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FILING DATE.**

APPLICATION NUMBER: 60/414,647

FILING DATE: October 01, 2002

RELATED PCT APPLICATION NUMBER: PCT/US03/31089



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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

INVENTOR(S)

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☒ Additional inventors are being named on the 1 separately numbered sheets attached hereto

TITLE OF THE INVENTION (280 characters max)

URINE BIOCHEMICAL MARKERS OF RENAL TRANSPLANT REJECTION BASED ON MOLECULAR MASS PEAKS

Direct all correspondence to:

CORRESPONDENCE ADDRESS

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Patent Application Number
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30743

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ENCLOSED APPLICATION PARTS (check all that apply)

☒ Specification Number of Pages 19

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☒ Drawing(s) Number of Sheets 113

☐ Other (specify)

☐ Application Data Sheet. See 37 CFR 1.76

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT (check one)

☒ Applicant claims small entity status. See 37 CFR 1.27

☒ A check or money order is enclosed to cover the filing fees

☒ The Commissioner is hereby authorized to charge filing fees or credit any overpayment to Deposit Account Number 50-2041

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\$80.00

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government

☒ No

☐ Yes, the name of the U.S. Government agency and the Government contract number are:

Respectfully submitted,

SIGNATURE

Ruth E. Tyler-Cross

Date

9/30/02

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Docket Number:

03940067PR

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

This collection of information is required by 37 CFR 1.51. The information is used by the public to file (and by the PTO to process) a provisional application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 8 hours to complete, including gathering, preparing, and submitting the complete provisional application to the PTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Box Provisional Application, Assistant Commissioner for Patents, Washington, D.C.

P19SMALL/REV05

PROVISIONAL APPLICATION COVER SHEET
Additional Page

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Docket Number		03940067PR	Type a plus sign (+) inside this box →	+
INVENTOR(S)/APPLICANT(S)				
Given Name (first and middle (if any))	Family or Surname	Residence (City and either State or Foreign Country)		
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Number 2 of 2

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**CHARACTERIZATION OF RENAL TRANSPLANT REJECTION USING
URINARY SURROGATE MARKERS**

New minimally invasive methods of monitoring kidney transplant rejection are needed. Rejection continues to be the major impediment to the success of renal transplantation. Successful management requires early detection and adequate treatment. Available diagnostic methods include clinical presentation, biochemical parameters, and tissue biopsies. The first two are not infallible. The latter are costly, invasive, and have associated morbidity and mortality. As a result, biopsies are not performed on a routine basis despite their potential diagnostic benefits. Two events are thus observed: rejection is many times detected in advanced stages of progression, or subclinical rejection is not diagnosed. In either case, irreversible allograft injury occurs.

We developed a new non-invasive technology, with no morbidity or mortality, that will allow early detection of renal pathologies such as rejection and delayed graft function. This technique can be used for routine postoperative screening in cases of delayed graft function, especially in instances where extended criteria donors are used.

Molecular characterization of transplant rejection is a complex process involving identification of biomolecules of interest, profiling of differences in these biomolecular populations between normal and diseased states, and investigation into which ones are associated with rejection. A molecule that accurately reflects a diseased state can be defined as a biomarker. Biomarkers can be used both to elucidate the mechanism of rejection, or as early warning signs for the onset of rejection that prompt intervention therapy.

This invention centers on urine and urinary sediment as the substrates for diagnostic examination. Urine offers several advantages over any other specimen: collection is risk-free, non-invasive, and involves no discomfort to the patient. Unlike biopsies, urine and its sediment allow for sampling of the entire organ and therefore should more accurately reflect its physiologic state and level of function.

We have identified 47 potential biomarkers of renal transplant rejection in urine based on an area under the curve (AUC) > 0.6 for a receiver operating characteristic (ROC) curve. The potential markers were found to have molecular weights of 2.6, 3.4, 3.5, 3.8, 4.1, 4.7, 4.8, 5.0, 5.5, 5.6, 6.1, 6.4, 6.5, 6.6, 6.7, 6.8, 7.0, 7.1, 7.3, 7.5, 7.8, 8.0, 8.1, 9.0, 9.1, 9.3, 9.6, 9.7, 9.8, 10.0, 10.8, 10.9, 11.3, 13.4, 13.9, 14.7, 14.8, 15.1, 15.2, 16.1, 25.0, 28.0, 50.0, 50.1, 51.1, 51.3, 67.0 kilodaltons (kD) as determined by surface enhanced laser desorption ionization (SELDI) mass spectrometry.

Rejection constitutes the major impediment to the success of solid organ transplantation. Adequate management of patients requires early detection of rejection and appropriate treatment. Current available methods, including clinical presentation and biochemical parameter, often fail to detect rejection until late stages of progression. Renal biopsies currently represent the most accurate way of diagnosis, but they have associated morbidity and mortality and provide only a limited sample of the organ. Development of biomarkers of rejection in urine represents a new non-invasive technology, with no morbidity or mortality that would allow for the early detection of renal allograft rejection.

Current methods of detecting transplant rejection, specifically needle biopsy, are invasive and can lead to increased risk of morbidity and mortality in the patient. Our approach utilizes biomarker in urine, which involved non-invasive specimen collection and does not lead to increased risk in the patient. In addition, urine passes through entire kidney so the urine specimen is a representative sample of the entire organ, where a needle biopsy provides only a limited sample of the organ.

References

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- Steinhoff J, Einecke G, Niederstadt C, Fricke L, Rob PM, Sack K. Myeloperoxidase in urine: a new marker for distinction between rejection and urinary tract infection after renal transplantation. Transplant Proc, 29 (1997) 3098.
- Roberti I, Reisman L. Serial evaluation of cell surface markers for immune activation after acute renal allograft rejection by urine flow cytometry - correlation with clinical outcome. Transplantation, 71 (2001) 1317.

All references cited in this provisional patent application are herein incorporated by reference, each in its respective entirety.

The described technology can be used to detect acute renal transplant failure. It can also prevent chronic renal transplant failure by detecting acute renal transplant failure. The invention covers a method to examine proteins in the urine for the presence of proteins indicating renal transplant failure. The identification of those proteins are included in the supporting material. The described technology will allow for the distinction between kidney transplant failure from delayed function of the kidney as well as from other renal pathologies. The described method will allow for the physician to decrease or even discontinue immuno-suppression; therefore, preventing side effects of immuno-suppression. The described method will allow for the close monitoring of ideal and extended criteria kidney transplants with no or minimal morbidity. The described method will allow for the early identification and treatment of rejection, thereby prolonging the survival of the transplanted kidney. The described method will allow for the sampling of the kidney in its entirety rather than a very limited region such as occurs with biopsy samples. The described method will allow the physician to provide appropriate treatment if the urine indicates that acute rejection is occurring to try to prevent loss of or injury to the kidney. Such detection may occur at any stage of rejection, even at early points not identified by kidney biopsy or laboratory blood testing. The described method will allow for the development and use of antibodies directed against the urinary markers described and their use for the detection and identification of renal rejection, delayed graft function, and other pathologies. The described method can be used for any species where kidney transplants occur including but not limited to humans, dogs, cats, and rats. The described method can also detect kidney transplant failure in transplants from the same species and also different species, any kidney that is transplanted.

Proteomic characterization of renal transplant rejection using Surface Enhanced Laser Desorption/Ionization (SELDI) and ProteinChipTM technology

Background

Since the first kidney transplant in 1954, transplantation has grown from an experimental procedure to an acceptable and widely used treatment for kidney failure. One drawback to this procedure, however, is the problem of acute transplant rejection or infection. Despite anti-rejection and immuno-suppression therapies, a significant number of organ transplant patients still experience acute rejection. Approximately 60% of kidney transplant patients will have at least one rejection episode in the first year after surgery. Fortunately, with medical treatment, about 90% of these cases are treated successfully. Optimal treatment, however, requires early detection and treatment of the transplant rejection. Available methods include clinical presentation, organ function parameters, and tissue biopsies, which are costly, invasive, and uncomfortable to the patient. As a result, these methods are performed infrequently, and rejection may not be detected until late stages of progression. New minimally invasive methods of monitoring kidney transplants are needed, which allow early detection and treatment of rejection patients.

Molecular characterization of transplant rejection is a complex process involving identification of biomolecules of interest, profiling of differences in these biomolecule populations between normal and diseased states, and investigation into which of these players contributes to transplant rejection. A molecule that accurately reflects a diseased state can be defined as a biomarker. Biomarkers can be used both to elucidate the mechanism of rejection, or as early warning signs for the onset of rejection that prompt intervention therapy. A Center for Biomarker Discovery has recently been established at Johns Hopkins for the identification of biomarkers in various diseases using state-of-the-art proteomic methods including SELDI-mass spectrometry.

Traditionally, biomarker discovery and validation involves separation and purification of the marker from the sample matrix, identification of the marker, characterization, and assay development, with each aspect being carried out in a different experiment or lab. Using SELDI-MS, biomarker discovery is accomplished at an accelerated pace by combining these steps into a simplified procedure performed on a 'chip' surface. Biological samples are incubated on a ProteinChip™ that possesses a specific surface chemistry. These chips can have various chromatographic surfaces including non-polar (RP), polar (NP), metal affinity (IMAC), anion (SAX2) or cation (WCX2) exchange, or immobilized biological ligands for bioaffinity interactions. Proteins that are not bound to the surface are washed away prior to sample analysis by time-of-flight mass spectrometry. This methodology can be used to compare two different sample sets (e.g. normal and diseased) to perform differential protein expression mapping and identify potential biomarkers. The need for improvement in early detection of transplant rejection is supported by the increasingly large prevalence of end-stage renal disease (ESRD) in the United States. The United States Renal Data System (USRDS) 2001 Annual Data Report indicates a point prevalence of 344,094 patients in 1999. Between 1984 and 1999, the annual number of kidney transplants performed more than doubled. As of October 1, 2001, 50,004 patients were on a waiting list for kidney transplantation [United Network for Organ Sharing]. Clearly, with increasing numbers of patients and medical costs, a high success rate of organ transplantation is desirable and may be facilitated by new methods of detecting transplant rejection and infection. The ideal characteristics of a detection method will include low levels of risk and discomfort to the patient. Rejection biomarkers seem ideally suited to the challenge of early, non-invasive recognition of transplant rejection patients.

Studies Related to New Invention

We used SELDI-MS employing ProteinChip™ technology (Ciphergen Biosystems, Palo Alto, CA) to screen urine samples from renal transplant patients for novel proteins produced

during post-transplant monitoring. Patients were divided into groups based on whether the donor is live or cadaveric. Initial studies involved optimization of chip technology for biomarker discovery in urine. A standardized protocol, the rapid screening capabilities of SELDI-MS, will be utilized to analyze protein profiles of transplant patients at various stages of recovery or rejection. We used the differential protein expression profiles generated from SELDI-MS to generate graphical comparison maps for identification of potential biomarkers of rejection. Once a promising biomarker was identified, purification for further analyses was performed using liquid chromatography or the ProteinChipTM surfaces.

Proteins unique to the first stages of rejection may serve as early indicators of acute rejection or infection, or as markers of risk for chronic rejection. However, these proteins are useful only if they are applied clinically as predictive biomarkers. To apply these biomarkers for clinical diagnostic or prognostic uses, rapid and inexpensive assays must be developed. The advantage of using SELDI-MS is that protein purification, characterization, and identification can all be carried out on the same chip, using a single instrument and only a few microliters of sample. This should drastically reduce the amount of time needed to optimize an analyte-specific assay.

Additionally, protein patterns, or "signatures", can be used as markers themselves instead of identifying a specific component. Using software developed at the Center for Biomarker Discovery, the utility of using protein pattern recognition as a marker for rejection will be investigated. A sample set containing both known normal and rejection samples were used as a training set to determine the parameters needed for pattern recognition. Once the pattern was determined, a blinded sample set was used to validate the pattern for use as a composite "biomarker". Both approaches to biomarkers were investigated as a viable and less invasive alternative to kidney biopsy for diagnostic and prognostic evaluation of transplant rejection.

Urine Specimen Processing

- Urine samples were collected from 32 renal transplant patients at various stages of post-transplant recovery or rejection. 25 samples were collected from rejection patients, and 15 samples were collected from non-rejection patients, with 2 patients contributing matched urine specimens (both pre-rejection and post-rejection).
- Patients' transplant rejection status was confirmed by kidney biopsy.
- Specimens were centrifuged for 5 minutes at 1000 g to remove sediment. Supernatants were aliquoted and frozen at -80° C.

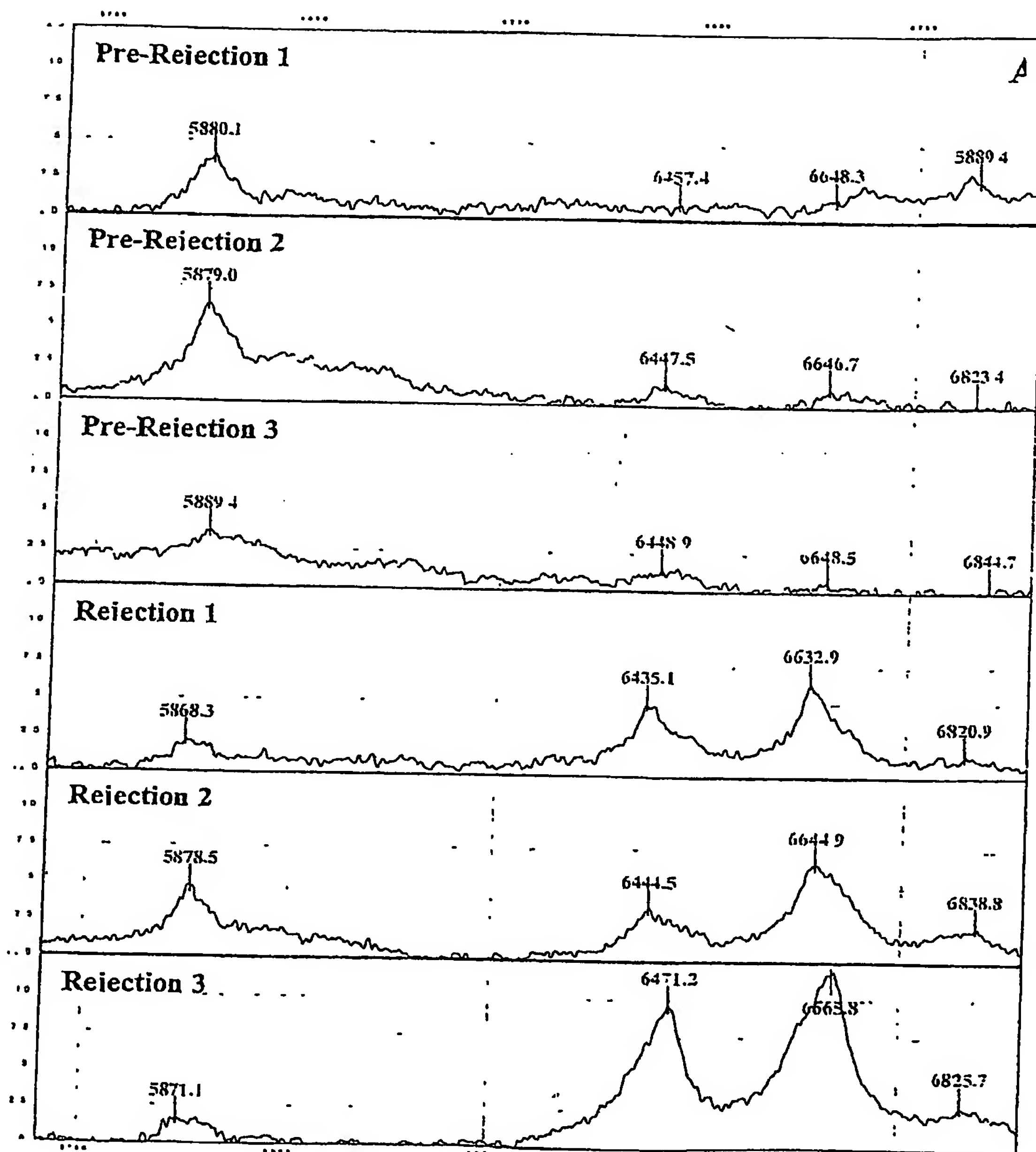
SELDI Mass Spectrometry

- Processed urine samples were applied in triplicate to SELDI ProteinChip® Arrays, with metal affinity (IMAC-3) and hydrophobic (H₄) chemistry. IMAC-3 chips had been pretreated with 100mM CuSO₄ and PBS. H₄ chips had been pretreated with 50% Acetonitrile
- 3 mL of urine were added to each chip spot in duplicate. Chips were incubated at 37° C between applications, allowing samples to dry on the chip surface.
- Specimens were applied to chips in a random pattern, in order to minimize the effects of spot to spot variation.
- Following sample application, IMAC-3 chips were washed with PBS and H₄ chips were washed with 20% Acetonitrile.
- CHCA (alpha-cyano-4-hydroxycinnamic acid) or SPA (sinapinic acid) matrix solution (composed of energy absorbing molecules) was then added to each chip spot in duplicate.
- Protein chips were analyzed on a PBS-II mass reader (Ciphergen Biosystems, Fremont, CA) with SELDI 3.0 software. Data were collected by averaging 110 laser shots with intensities and detector sensitivities optimized for each combination of chip and matrix type.

Data Analysis

- Mass spectra generated by SELDI mass spectrometry analysis were examined visually to select peaks with potential to distinguish between pre-rejection and rejection patients.
- SELDI software was used to identify all peaks in the spectrum data by applying a threshold to signal-to-noise values.
- Labeled peaks were normalized to the Creatinine content of each urine specimen, through division of peak intensity by Creatinine concentration in g/dL. Outliers were removed from the triplicate data sets based on the results of Tn tests.
- Both visually and computer labeled peaks were analyzed with ProPeak software to statistically identify those peaks with the best ability to distinguish between the patient populations. Peak intensities were log normalized for ProPeak analysis.
- ProPeak software used UMSA (Unified Maximum Separability Analysis) to identify a direction in n-dimensional space along which two data sets are optimally separated. Bootstrap selection ranked peaks according to the strength and consistency of their ability to discriminate between the sets.
- The diagnostic performance of highly ranked peaks from UMSA analysis was evaluated by receiver operating characteristic (ROC) analysis. The ability of the peaks to distinguish between pre-rejection and rejection patients was ranked by the area under the ROC curve (AUC). Peaks with AUCs greater than 0.6 were classified as peaks of interest, the highest of which (AUCs > 0.75) are candidate biomarkers.
- Computer labeled peaks were subjected to CART (Classification and Regression Tree) analysis, implemented by Ciphergen Biomarker Patterns Software[®], in order to identify patterns of biomarkers which distinguish between patient populations.
- Samples from patients less than four days post-transplant (n=3) were omitted from data analysis, due to the presence of excessive inflammatory response proteins.

Sample Spectra



Acute Rejection Episodes: Earlier and More Frequent in Recipients of Extended Organ Donor Allografts

Background

- Increased use of extended organ donors
- Unknown incidence of acute rejection in this group has not been clearly defined:
 - No uniform definition of high risk patients
 - Most studies are retrospective
 - Numbers are small

Expanded Criteria Donors: Definition Used

- Age
 - ≤ 5 years
 - ≥ 55 years
- Terminal Creatinine ≥ 1.5 mg/dl
- History of Hypertension / Diabetes
- Cold Ischemia Time ≥ 30 hours

Aim

Compare the **timing** and **severity** of acute rejection episodes among extended criteria and non-extended criteria donors

Materials and Methods

Prospectively collected data from
351 consecutive cadaveric kidney
transplants performed at our
Institution

Immunosuppression (Kidney Alone)

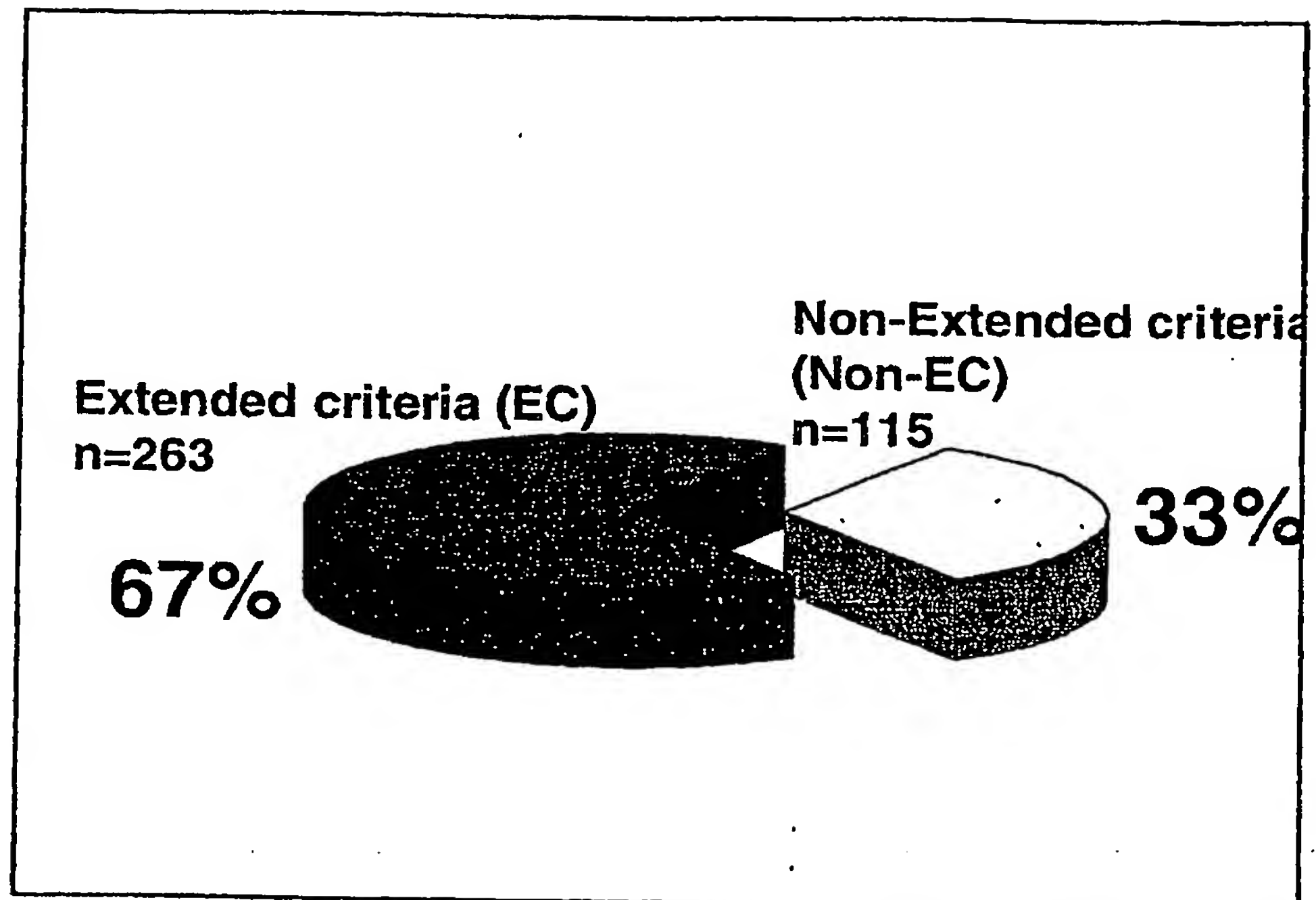
	Expanded Criteria	Other	p
Tacrolimus	94%	88%	NS
MMF	89%	86%	NS
IL2R ab	18%	3%	0.003
OKT3/ATG	12%	5%	0.09

Materials and Methods

- Acute rejection episodes were scored using Banff 97 criteria.
- Groups were compared using Fishers exact test or Pearson Chi Square (for variables with 3+ categories).

Materials and Methods

Follow-up was measured from transplantation to first episode of biopsy proven AR, and was censored at end of available follow-up or patient death; it was evaluated using the Kaplan Meier method and compared using log rank test



Donor Characteristics

p=ns

Recipient Characteristics

Results

- >382.2 graft years of follow-up (55% EC)
- 128 Biopsy proven Acute Rejections
 - 100 EC (42.4% event rate)
 - 28 Non-EC (24.3% event rate)

P=0.001

$\frac{F}{m} = \frac{1}{m} \left(\frac{1}{2} m v^2 \right) = \frac{1}{2} v^2$

- ## Acute Rejection
- Median acute rejection-free follow-up per patient: 0.55 yrs
 - Mean AR free survival (years)
 - 2.3 (0.6) for EC
 - 3.5 (0.2) Non-EC
- $P < 0.001$

Timing of Acute Rejection

Cumulative incidence of Acute Rejection
within the first 6 weeks post transplant:

EC	84%
Non-EC	57%

P=0.006

EC 84%

P=0.006

[illegible]

-35% EC

-16% Non-EC



Conclusions

These findings support the need for increased intensity or alterations of immunosuppressive strategies during the peri and early postoperative period.

LISTED PATIENTS-

- **Kidney: 49,442**
- **Pancreas: 1,173**
- **Kidney-Pancreas: 2,542**
- **Liver: 17,977**
- **Intestine: 168**
- **Heart: 4,230**
- **Heart-Lung: 222**
- **Lung: 3,753**

TOTAL: 77,179 (Multiple Organs)

TRANSPLANTS - 2000

- **Kidney Alone:13,372 (5,293 Live Donors)**
- **Pancreas Alone: 435**
- **Kidney-pancreas: 911**
- **Liver: 4,954**
- **Intestine: 79**
- **Heart: 2,198**
- **Heart-lung: 48**
- **Lung: 956**

Total: 22,953

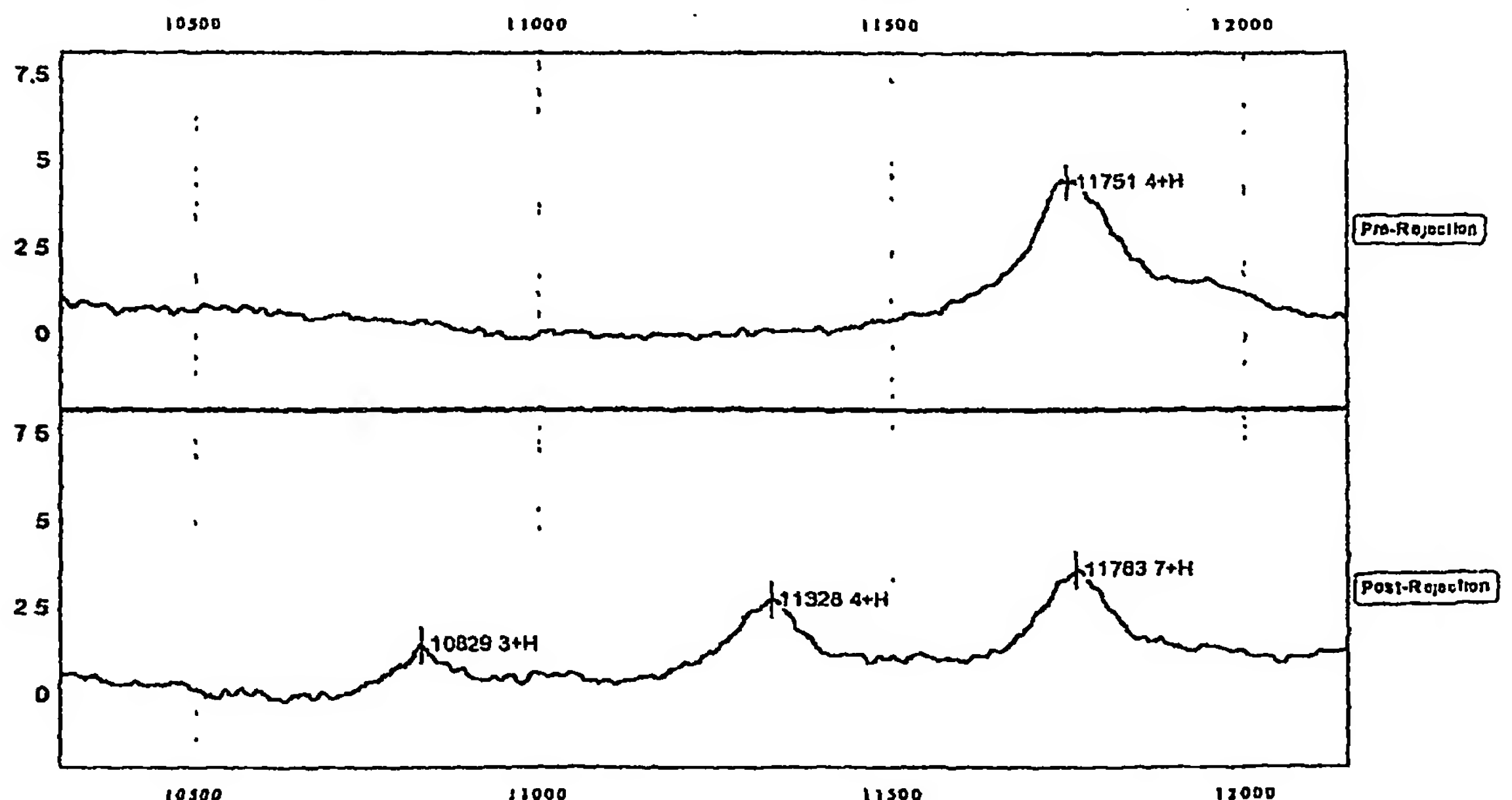
CHARACTERIZATION OF RENAL ALLOGRAFT REJECTION BY MEANS OF SURFACE ENHANCED LASER DESORPTION/IONIZATION (SELDI) MASS SPECTROMETRY AND URINARY PROTEOMIC ANALYSIS

Background: Rejection constitutes the major impediment to the success of transplantation. Adequate management requires early detection and appropriate treatment. Current available methods, including clinical presentation and biochemical parameters, often fail to detect rejection until late stages of progression. Although renal biopsy currently represents the most accurate way of diagnosis, it is costly, invasive, has associated morbidity and mortality, and provides only a limited sample of the organ.

Aim: Our goal was to develop a new non-invasive technology, with no morbidity or mortality that would allow for the early detection of renal allograft rejection.

Methods: Urine samples were prospectively collected from 32 renal transplant recipients at various time periods after transplantation. Twenty-two samples were collected from patients with acute cellular rejection. Eighteen samples were obtained from recipients with no rejection. Six patients contributed matched urine specimens (both pre-rejection and post-rejection). The presence and diagnosis of acute cellular rejection was confirmed by renal biopsy in all cases. Proteins of interest were captured on a protein biochip of specific surface chemistry, and were subsequently ionized by excitation with a laser source. The resulting ions were characterized with a time-of-flight analyzer. Data generated by SELDI mass spectrometry were compared by differential protein profiling and analyzed using ProPeak software.

Results: Analysis of the samples collected revealed fifteen protein peaks of approximately 3.4, 4.8, 5.0, 5.3, 5.6, 6.1, 6.4, 7.0, 7.3, 7.7, 10.8, 11.3, 13.4, 14.6, and 50.2 kD which were unique to urine specimens from recipients with acute cellular rejection. These protein peaks were absent in specimens from recipients with no evidence of acute cellular rejection or in whom it had been treated successfully. Further characterization of these protein peaks is illustrated below, where pre- and post-rejection urine specimens are compared.



Conclusions: Using Surface Enhanced Laser Desorption/Ionization (SELDI) mass spectrometry we were able to identify characteristic protein peaks present in urinary specimens of renal transplant recipients. Our results identified several peaks present in the urine of patients with acute cellular rejection that disappear in its absence. To the best of our knowledge, this is the first successful proteomic characterization of renal transplant rejection by means of urinary biomarkers. Further use of these biomarkers could allow for routine screening of renal transplant patients, the early detection of allograft rejection, and the ability to differentiate rejection from other renal pathologies by means of a non-invasive technique with no associated morbidity or mortality.

Proteomic Characterization of Renal Transplant Rejection Using Surface Enhanced Laser Desorption/Ionization (SELDI) Mass Spectrometry

The most serious problem faced by renal transplant patients is the occurrence of acute rejection, an aggressive immune response often responsible for organ loss. Early detection of renal transplant rejection, an essential step for optimal treatment, is challenging. Available methods, including clinical presentation, organ function parameters, and tissue biopsies, often fail to detect rejection until late stages of progression. An understanding of the molecular events leading to transplant rejection is crucial to developing new methods of monitoring kidney transplants and improving treatments of patients. Characterization of transplant rejection is a complex process involving identification of biomolecules of interest and determination of differences in these biomolecule populations between normal and diseased states. Molecules directly reflecting a diseased state can be defined as biomarkers and may be used both to elucidate the mechanism of transplant rejection and as early warning signs of rejection. We are using Surface Enhanced Laser Desorption/Ionization (SELDI) mass spectrometry (Ciphergen Biosystems, Fremont, CA) for proteomic analysis of urine samples from renal transplant patients. Traditionally, biomarker discovery and validation involves separation and purification of the marker from the sample matrix, identification of the marker, characterization, and assay development, with each step being carried out in different experiments or laboratories. SELDI mass spectrometry accelerates this discovery process by combining these steps into a simplified procedure performed on a ProteinChip® Array. Proteins of interest are captured onto a chip with a specific surface chemistry by incubation with biological source material and are then ionized directly on the chip surface by excitation from a laser source. Resulting ions are characterized with a time-of-flight analyzer. A particular advantage of this methodology is the ease of comparing different sample sets, such as normal and diseased conditions, through differential protein expression mapping. In this study, urine samples were collected from 6 renal transplant patients at various stages of post-transplant recovery or rejection. Each patient served as a normal (pre-rejection) and diseased (post-rejection) subject. The patients' transplant rejection status was determined by kidney biopsy. Data generated by SELDI mass spectrometry from pre- and post-rejection patients were compared by differential protein profiling. Preliminary results from 3 patients who experienced transplant rejection episodes showed two protein peaks of approximately 11.7 kD and 13.9 kD which were present in post-rejection urine samples but absent in pre-rejection specimens from the same patients. In addition, the results indicated one protein peak of approximately 15.1 kD which was present in pre-rejection patient samples but disappeared after onset of rejection. Identification of these protein peaks will establish biomarkers and potential therapeutic targets for renal transplant rejection. Such rejection biomarkers seem ideally suited to face the challenge of early, non-invasive recognition of transplant rejection.

ABSTRACT

The most serious problem faced by renal transplant patients is the occurrence of acute rejection, an aggressive immune response often responsible for organ loss. Early detection of renal transplant rejection, an essential step for optimal treatment, is challenging. Available methods, including clinical presentation, organ function parameters, and tissue biopsies, often fail to detect rejection until late stages of progression. An understanding of the molecular events leading to transplant rejection is crucial to developing new methods of monitoring kidney transplants and improving treatments of patients. Characterization of transplant rejection is a complex process involving identification of biomolecules of interest and determination of differences in these biomolecule populations between normal and diseased states. Molecules directly reflecting a diseased state can be defined as biomarkers and may be used both to elucidate the mechanism of transplant rejection and as early warning signs of rejection. We are using Surface Enhanced Laser Desorption/Ionization (SELDI) mass spectrometry (Ciphergen Biosystems, Fremont, CA) for proteomic analysis of urine samples from renal transplant patients. Traditionally, biomarker discovery and validation involves separation and purification of the marker from the sample matrix, identification of the marker, characterization, and assay development, with each step being carried out in different experiments or laboratories. SELDI mass spectrometry accelerates this discovery process by combining these steps into a simplified procedure performed on a ProteinChip® Array. Proteins of interest are captured onto a chip with a specific surface chemistry by incubation with biological source material and are then ionized directly on the chip surface by excitation from a laser source. Resulting ions are characterized with a time-of-flight analyzer. A particular advantage of this methodology is the ease of comparing different sample sets, such as normal and diseased conditions, through differential protein expression mapping. In this study, urine samples were collected from 32 renal transplant patients at various stages of post-transplant recovery or rejection. 25 samples were collected from rejection patients, and 15 samples were collected from non rejection patients, with 2 patients contributing matched urine specimens (both pre-rejection and post-rejection). The patients' transplant rejection status was determined by kidney biopsy. Data generated by SELDI mass spectrometry from pre- and post-rejection patients were compared by differential protein profiling and analyzed using ProPeak software (32 Informatics, Mount Pleasant, SC), Receiver Operating Characteristic (ROC) curves, and Ciphergen Biomarker Patterns Software®. Results showed ten protein peaks of approximately 3.4, 4.1, 6.5, 6.6, 6.7, 7.0, 7.1, 7.3, 7.5, and 13.4 kD which were present in a majority of post-rejection urine samples but absent in most of the pre-rejection specimens. In addition, the results indicated five protein peaks of approximately 9.0, 9.6, 9.7, 9.8 and 10.0 kD which were present in most pre-rejection patient samples but were down regulated after onset of rejection. Identification of these protein peaks will establish potential biomarkers and possible therapeutic targets for renal transplant rejection. Such rejection biomarkers seem ideally suited to face the challenge of early, non-invasive recognition of transplant rejection.

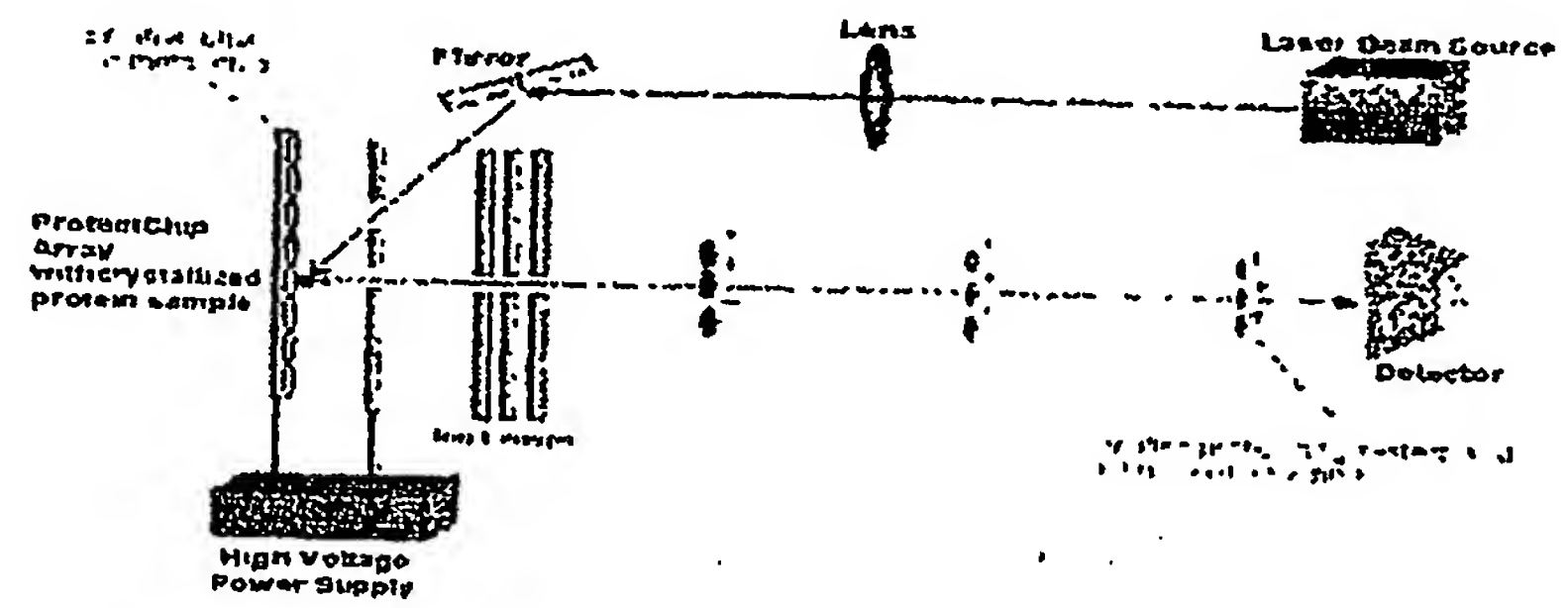
Tables 1-3. Ranked Peaks of Interest (AUCs > 0.600).

Rank	Molecular Weight (kD)	AUC	p
H4 Chip with SPA Matrix (Laser Intensity = 200, Detector Sensitivity = 6)			
1	65	0.824	<0.0001
2	67	0.821	<0.0001
3	34	0.773	0.0002
4	70	0.764	0.0009
5	108	0.745	0.0026
6	81	0.742	0.0020
7	35	0.733	0.0029
8	68	0.730	0.0025
9	56	0.706	0.0107
10	98	0.697	0.0117
11	134	0.691	0.0188
12	91	0.682	0.0221
13	51.1	0.682	0.0258
14	61	0.636	0.0903
15	113	0.630	0.1091
16	147	0.609	0.1252
17	48	0.603	0.1466
H4 Chip with SPA Matrix (Laser Intensity = 250, Detector Sensitivity = 7)			
1	65	0.779	0.0002
2	98	0.776	0.0002
3	100	0.776	0.0002
4	41	0.715	0.0083
5	108	0.706	0.0152
6	34	0.688	0.0162
7	78	0.679	0.0261
8	134	0.679	0.0267
9	91	0.664	0.0329
10	35	0.655	0.0477
11	26	0.655	0.0502
12	73	0.645	0.0697
13	51.3	0.645	0.0704
14	48	0.633	0.0801
15	119	0.615	0.1313
16	147	0.612	0.1211
17	56	0.600	0.1648
Rank	Molecular Weight (kD)	AUC	p
H4 Chip with CHCA Matrix (Laser Intensity = 180, Detector Sensitivity = 6)			
1	97	0.809	<0.0001
2	41	0.788	0.0002
3	66	0.776	0.0002
4	90	0.758	0.0006
5	67	0.733	0.0025
6	35	0.715	0.0061
7	50.0	0.703	0.0140
8	34	0.691	0.0150
9	65	0.683	0.0191
10	64	0.667	0.0348
11	50	0.661	0.0433
12	56	0.658	0.0675
13	108	0.652	0.0635
14	70	0.648	0.0676
15	25.0	0.639	0.0675
16	93	0.618	0.1046
17	47	0.612	0.1176
18	61	0.606	0.1557
H4 Chip with CHCA Matrix (Laser Intensity = 210, Detector Sensitivity = 6)			
1	98	0.812	<0.0001
2	96	0.758	0.0005
3	90	0.715	0.0074
4	47	0.703	0.0109
5	26	0.691	0.0147
6	50.1	0.624	0.0993
7	65	0.621	0.0971
8	61	0.618	0.1382
9	28.0	0.603	0.1401
10	15.1	0.603	0.1604
11	70	0.603	0.1689
Rank	Molecular Weight (kD)	AUC	p
IMAC Chip with SPA Matrix (Laser Intensity = 240, Detector Sensitivity = 8)			
1	71	0.806	<0.0001
2	70	0.788	<0.0001
3	73	0.773	0.0008
4	75	0.773	0.0009
5	80	0.748	0.0029
6	134	0.742	0.0017
7	148	0.733	0.0048
8	10.9	0.691	0.0092
9	34	0.688	0.0190
10	15.2	0.685	0.0263
11	78	0.676	0.0382
12	55	0.615	0.1179
13	16.1	0.614	0.1305
IMAC Chip with CHCA Matrix (Laser Intensity = 180, Detector Sensitivity = 9)			
1	13.4	0.782	<0.0001
2	78	0.742	0.0049
3	38	0.739	0.0036
4	71	0.733	0.0035
5	70	0.730	0.0028
6	35	0.724	0.0038
7	48	0.700	0.0121
8	15.2	0.685	0.0265
9	67	0.661	0.0425
10	67.0	0.658	0.0445
11	10.8	0.655	0.0484
12	34	0.615	0.1137
13	98	0.607	0.1560

INTRODUCTION

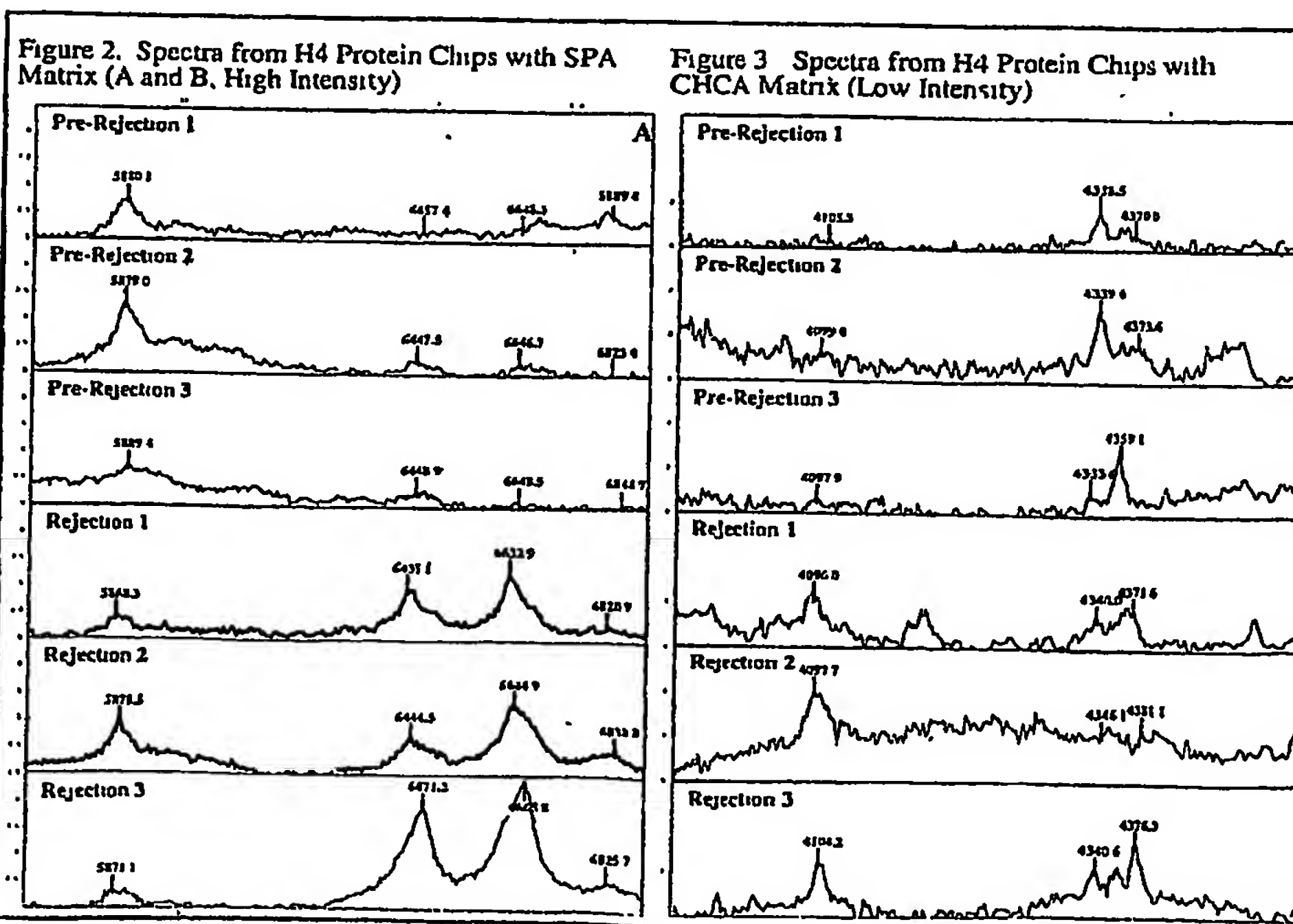
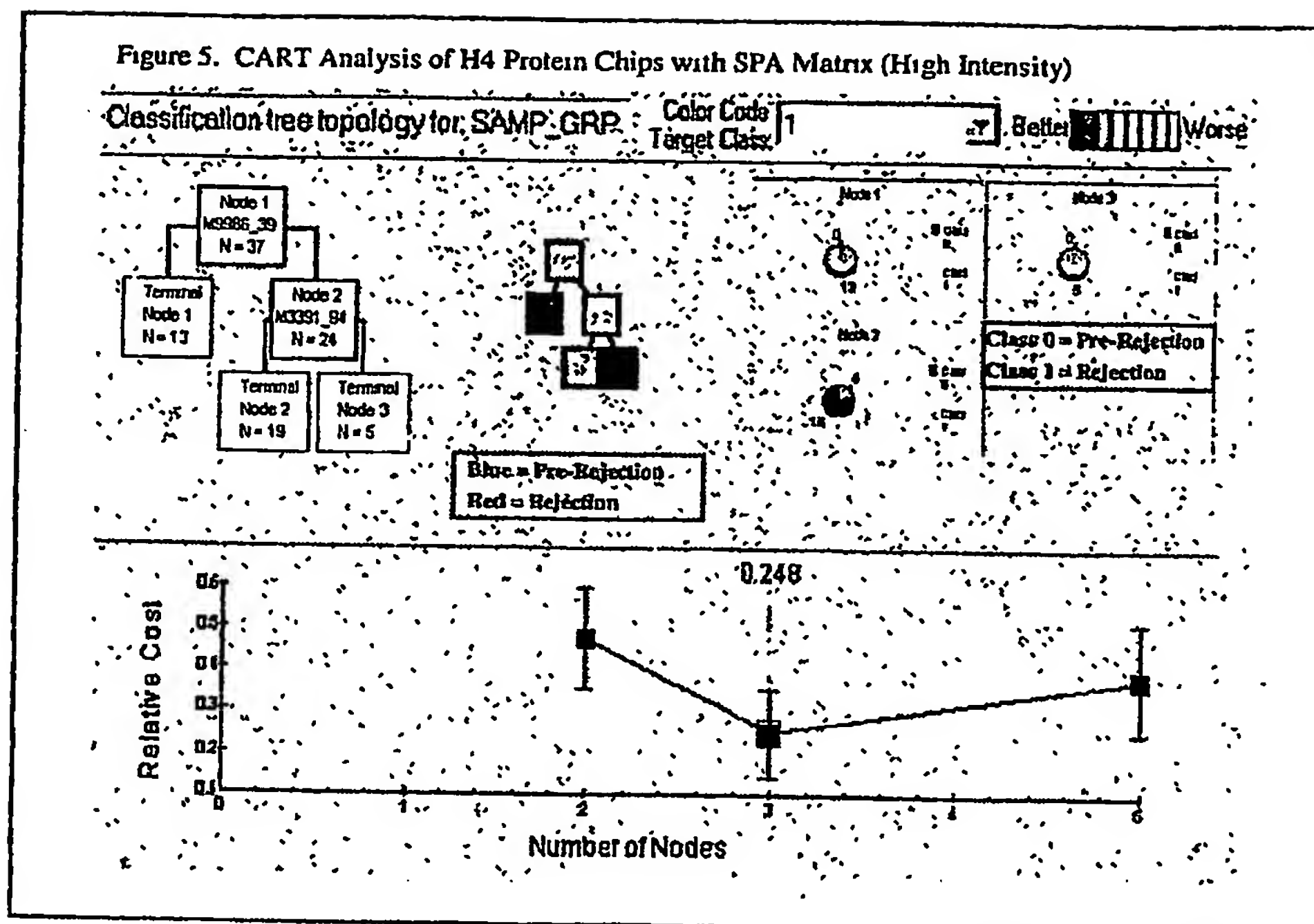
- The most serious impediment to the success of renal transplantation is the occurrence of acute rejection, an aggressive immune response often responsible for organ loss
- Adequate management of renal transplant rejection requires early detection and appropriate treatment. Current available methods, including clinical prevention, biochemical parameters, and tissue biopsies, often fail to detect rejection until late stages of progression
- Renal biopsies are currently the most accurate way of diagnosis, but have associated morbidity and mortality and provide only a limited sample of the organ
- The purpose of this study is to develop non-invasive methods for the diagnosis of renal transplant rejection, based on the discovery of novel biomarkers in urine specimens from renal transplant patients using SELDI™ mass spectrometry

Figure 1 Schematic of SELDI™-MS Protein Chip Reader
Schematic of ProteinChip Reader



Tables 1-3 Ranked Peaks of Interest (AUCs > 0.600)

Rank	Peak #	Peak Name	AUC	Rank	Peak #	Peak Name	AUC	Rank	Peak #	Peak Name	AUC
1	1	1.0	0.95	1	1	1.0	0.95	1	1	1.0	0.95
2	2	2.0	0.90	2	2	2.0	0.90	2	2	2.0	0.90
3	3	3.0	0.85	3	3	3.0	0.85	3	3	3.0	0.85
4	4	4.0	0.80	4	4	4.0	0.80	4	4	4.0	0.80
5	5	5.0	0.75	5	5	5.0	0.75	5	5	5.0	0.75
6	6	6.0	0.70	6	6	6.0	0.70	6	6	6.0	0.70
7	7	7.0	0.65	7	7	7.0	0.65	7	7	7.0	0.65
8	8	8.0	0.60	8	8	8.0	0.60	8	8	8.0	0.60
9	9	9.0	0.55	9	9	9.0	0.55	9	9	9.0	0.55
10	10	10.0	0.50	10	10	10.0	0.50	10	10	10.0	0.50
11	11	11.0	0.45	11	11	11.0	0.45	11	11	11.0	0.45
12	12	12.0	0.40	12	12	12.0	0.40	12	12	12.0	0.40
13	13	13.0	0.35	13	13	13.0	0.35	13	13	13.0	0.35
14	14	14.0	0.30	14	14	14.0	0.30	14	14	14.0	0.30
15	15	15.0	0.25	15	15	15.0	0.25	15	15	15.0	0.25
16	16	16.0	0.20	16	16	16.0	0.20	16	16	16.0	0.20
17	17	17.0	0.15	17	17	17.0	0.15	17	17	17.0	0.15
18	18	18.0	0.10	18	18	18.0	0.10	18	18	18.0	0.10
19	19	19.0	0.05	19	19	19.0	0.05	19	19	19.0	0.05
20	20	20.0	0.00	20	20	20.0	0.00	20	20	20.0	0.00



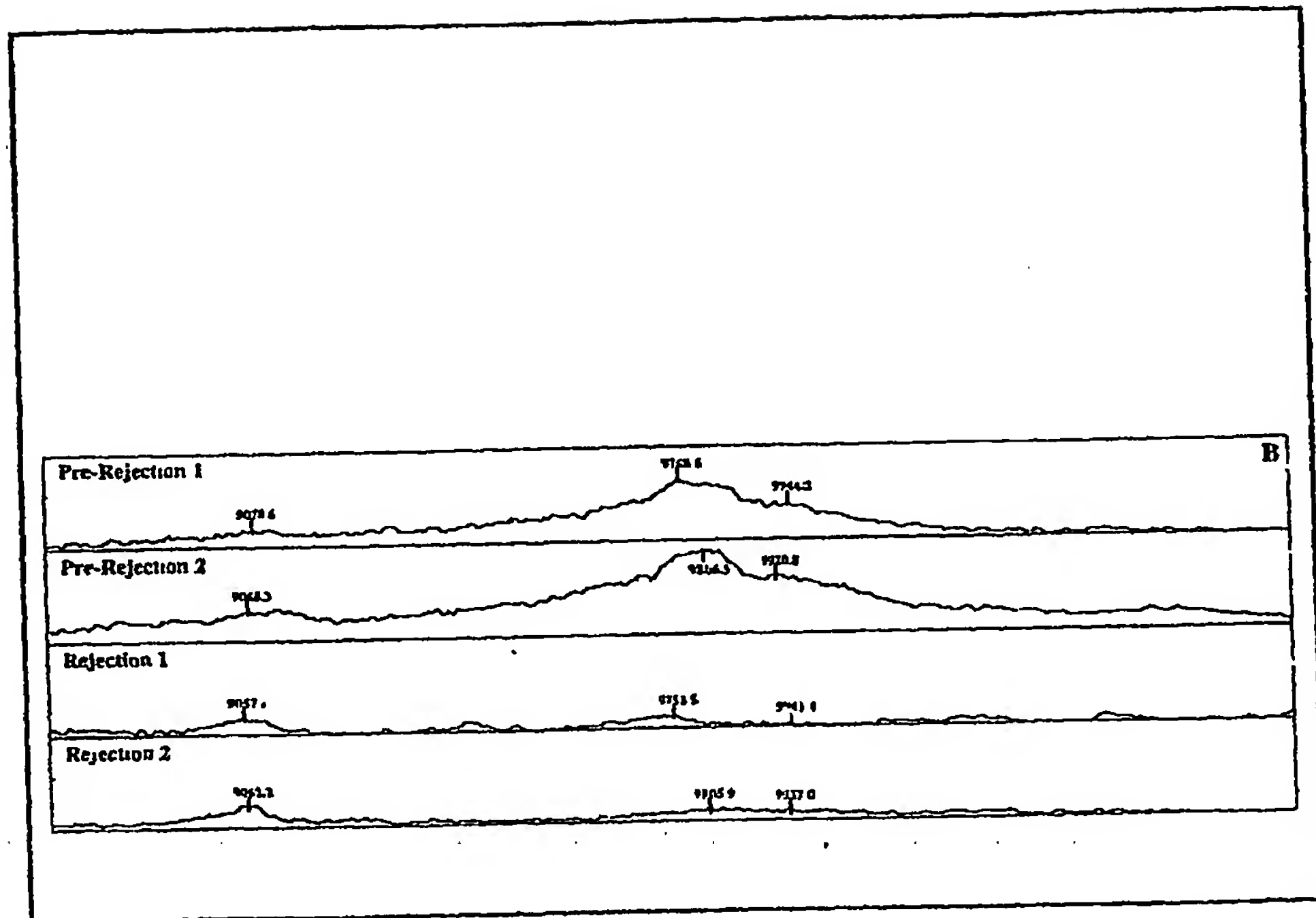


Figure 6 UMSA Analysis of Urine Samples on H4 Protein Chips with CHCA Matrix (Low Intensity) (A) All Peaks Computer Labeled and (B) Candidate Biomarkers (4.1, 6.6, and 9.7 kD)

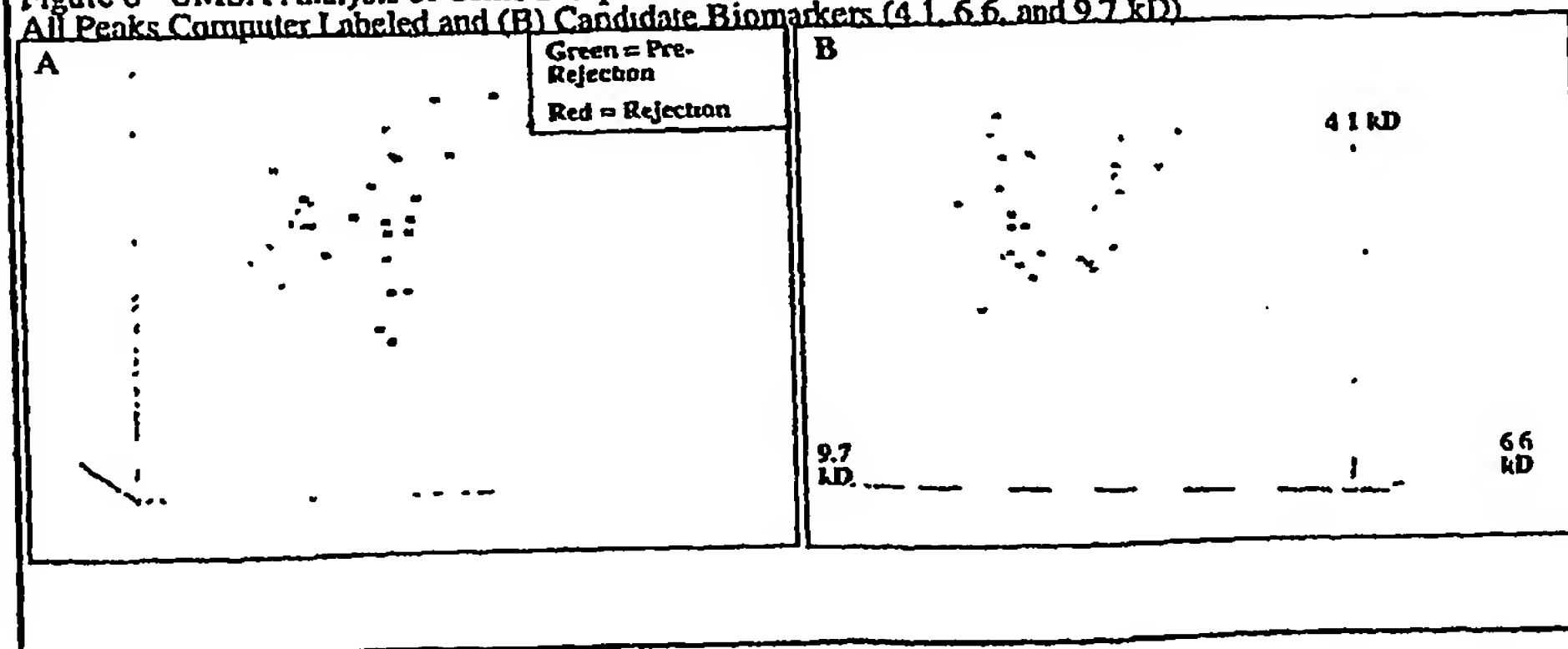
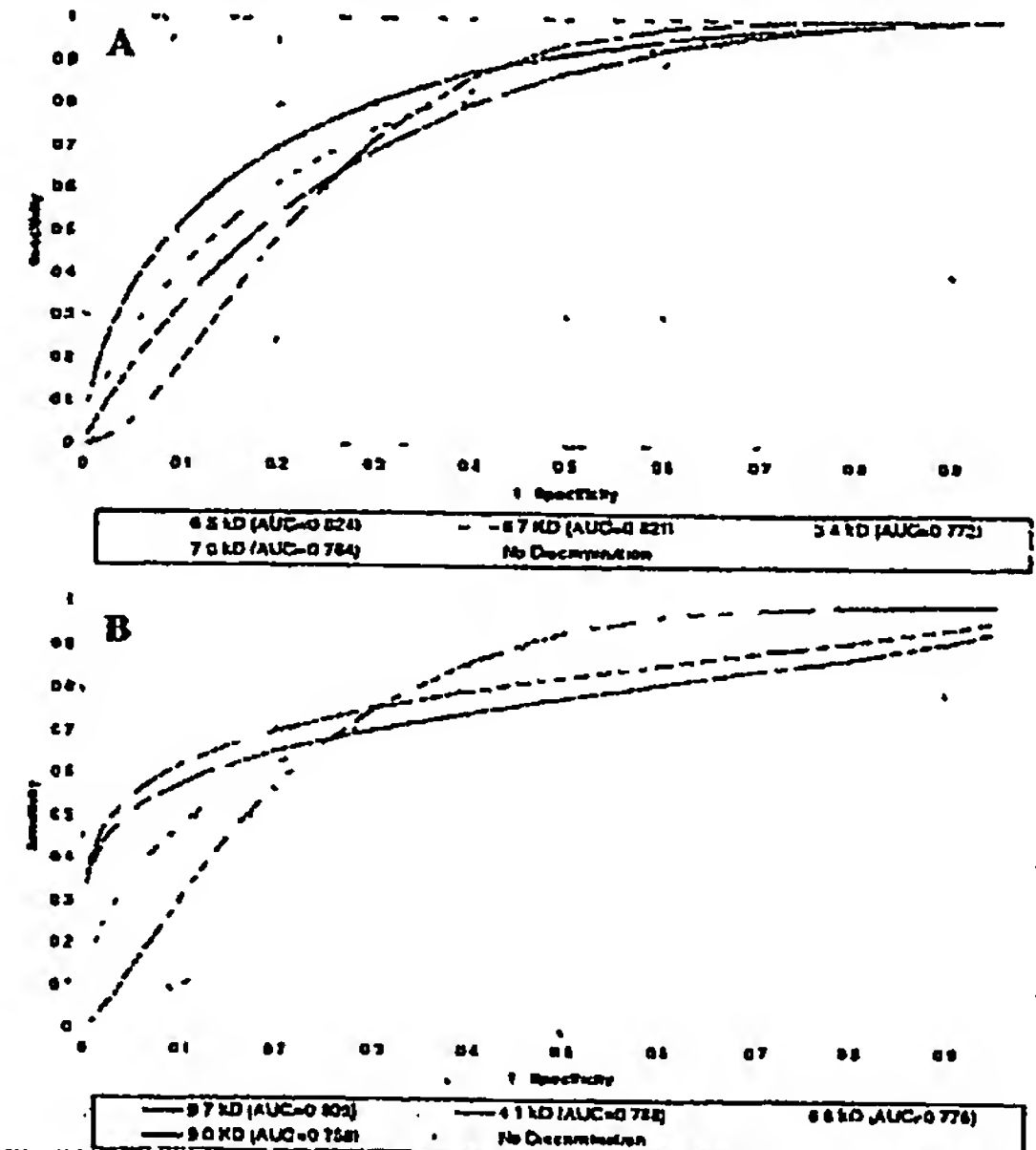


Figure 4. ROC Analysis of Candidate Biomarkers from H4 Protein Chips with (A) SPA and (B) CHCA Matrix (Low Intensity).



RESULTS

- Visual and UMSA analysis of spectra from renal transplant patients revealed 45 peaks of interest (AUCs > 0.600), which showed ability to distinguish between pre-rejection and rejection urine samples.
- Selected from these peaks of interest, 15 peaks (AUCs > 0.750 and p values < 0.0001 to 0.0009) showed promise as candidate biomarkers for transplant rejection. 10 of these peaks (3.4, 4.1, 6.5, 6.6, 6.7, 7.0, 7.1, 7.3, 7.5, and 13.4 kD) were present in a majority of post-rejection urine samples but absent from most pre-rejection specimens. 5 peaks (9.0, 9.6, 9.7, 9.8 and 10.0 kD) were down regulated with onset of transplant rejection.
- The best candidate biomarkers had highly successful diagnostic performance: 6.5 kD (AUC=0.824, p<0.0001), 6.7 kD (AUC=0.821, p<0.0001), 9.8 kD (AUC=0.812, p<0.0001), 7.1 kD (AUC=0.806, p<0.0001), and 13.4 kD (AUC=0.782, p<0.0001).
- CART analysis identified two of the same peaks (10.0 and 3.4 kD) which separated pre-rejection and rejection samples in a decision tree. This pattern correctly classified specimens in 89% of the training cases.

CONCLUSIONS

- A large numbers of peaks of interest had molecular weights within several percent of one another. The differences in weight were greater than the mass accuracy of the instrumentation ($<0.3\%$), preventing close peaks from being combined. Variations in chip surface chemistry and laser excitation (based on instrument settings and matrix type) may have accounted for the disparities. Spot to spot variation in the angle of incidence for laser desorption may have contributed additional discrepancies.
- We have identified potential biomarkers for renal transplant rejection, the most promising of which have masses of approximately 6.5, 6.7, 9.8, and 13.4 kDa.
- Combinations of peaks of interest through logistic regression will be used to determine if a panel of multiple markers results in improved diagnostic performance.
- Because the results of this study are limited by small sample size, a separate set of urine specimens from renal transplant patients will be used to validate the potential biomarkers. Identification and characterization of the candidate biomarkers will then be performed, followed by development of an analyte specific assay and clinical validation of that assay.

Handbook of Kidney Transplantation

Third Edition

Gabriel M. Danovitch



LIPPINCOTT WILLIAMS & WILKINS

Pathology of Kidney Transplantation

Cynthia C. Nast and Arthur H. Cohen

Structural abnormalities in the transplanted kidney may be assessed by either of two methods: (1) standard tissue histopathology of a biopsy or transplant nephrectomy or (2) cytologic evaluation of cells aspirated from the graft using a thin needle (Table 13.1). The core biopsy is typically regarded as the gold standard, whereas aspiration cytology, although clinically valuable and quite accurate in experienced hands, is somewhat limited as a procedure by the lack of trained clinicians to interpret the material. In this chapter, these techniques are considered separately, although the information obtained from them is often complementary, and certain important concepts and actual lesions described for one method bear directly on an understanding of the other.

KIDNEY TRANSPLANT HISTOPATHOLOGY

Core Needle Biopsy

Indications and Technique

Kidney transplant biopsies are most frequently performed at times of graft dysfunction when the etiology cannot be accurately elucidated by clinical or noninvasive means. Protocol biopsies are performed at predetermined intervals after transplantation at some centers in an attempt to recognize so-called subclinical rejection (see Chapter 8); they may also be required as part of clinical trials for the evaluation of new immunosuppressive drugs (see Chapter 4). More precise clinical indications for biopsy are reviewed in Chapters 8 and 9. Transplantation programs vary in their reliance on biopsies and the clinical setting in which biopsies are performed.

Preparations for transplant biopsy are similar to those for biopsy of the native kidney. Informed consent is required from patients who should be specifically warned of the risk for bleeding and organ damage to the graft (see Complications). Before biopsy, coagulation studies are usually performed, although in the absence of liver disease, use of anticoagulants, thrombocytopenia, or a clinical history of bleeding, these may not be necessary. The blood pressure should be controlled at a level of less than 160/100 mm Hg.

The locations of the graft and biopsy site can be determined by palpation or by ultrasound guidance. A small pillow or towel roll in the small of the patient's back may facilitate palpation. Ultrasound offers the advantage of more precise localization of the graft, and its depth, and may reduce the frequency of inadequate specimens. Ultrasound may detect perinephric fluid collections or hydronephrosis. It is unwise to perform biopsy through a fluid collection because of the inability to tamponade the biopsy site adequately. Significant hydronephrosis should be relieved before the

Table 13.1. Diagnostic capabilities of histologic and cytologic techniques for evaluation of kidney transplants

Lesion	Fine-needle Aspiration	Core Biopsy
Acute cellular rejection	Yes	Yes
Acute vascular rejection	No	Yes
Acute cyclosporine toxicity	Yes	Yes
Acute tubular necrosis	Yes	Yes
Viral infection	Yes	No
Allograft rupture	No	No
Bacterial infection	Yes	Yes
Infarction	Yes	Yes
Chronic transplant rejection	No	Yes
Chronic cyclosporine toxicity	No	Yes
Glomerular lesions	No	Yes
Recurrent nonglomerular disorders	No	Yes

biopsy is performed because it may be the cause of the graft dysfunction; a small blood clot after the biopsy may exaggerate the degree of obstruction. Generally, the upper or lower poles of the transplant are sought, depending on which is more easily palpated or near the surface. If the location of the biopsy site is difficult to ascertain or if the kidney is deep, it is wise to use real-time ultrasound with visual guidance or a fixed biopsy guide device (see Chapter 12).

Disposable automatic spring-loaded needles (18-gauge is usually adequate) have largely replaced the traditional modified 14-gauge Vim-Silverman needle and may be less traumatic to the kidney. The site chosen for the biopsy is locally anesthetized with 1% lidocaine, and a small stab wound in the skin is made to facilitate the passage of the needle. Precise instructions for use of the newer needles are provided in the package inserts. The needles are advanced up to the depth assigned by ultrasound or until an increase in resistance is felt as the needle makes contact with the kidney. When the automatic needles are used, it may be advisable to withdraw the needle slightly before taking the sample to avoid excessive depth. Two biopsy cores should be adequate. It is advisable to inspect the specimen immediately with a stereomicroscope to ensure adequacy. As soon as the needle is withdrawn, hemostasis should be augmented by manual compression or with a sandbag. Postbiopsy orders should include observation of the patient's vital signs every 15 minutes for at least 2 hours and then hourly for several hours. Patients should initially be immobile; in the absence of macroscopic hematuria, ambulation can begin after 6 to 8 hours. Many transplantation centers permit outpatients to go home the same day as the biopsy.

Complications

Core-needle biopsy is an invasive technique and is not risk free; these risks must be weighed against the benefit gained from the

information obtained from the procedure. Careful assessment of potential risks and benefits must precede every decision to subject a patient to a biopsy.

All major complications after needle biopsy manifest as perinephric or urinary bleeding. Transient macroscopic hematuria is common and is of little clinical significance. Macroscopic hematuria follows about 3% of biopsies and may prolong hospitalization or lead to blood transfusion or placement of a bladder catheter for clot drainage. Ureteral obstruction occasionally occurs, requiring placement of a percutaneous nephrostomy; massive hemorrhage necessitating surgical exploration, graft nephrectomy, or angiographic embolization is rare. Postbiopsy arteriovenous fistulas may sometimes be detected by Doppler ultrasound and can usually be treated expectantly. Angiographic embolization may occasionally be required, and graft loss has been reported.

Specimen Handling

Detailed methods for handling tissue specimens are beyond the scope of this chapter. For all specimens, portions are obtained for each of the three traditional methods of evaluating renal parenchyma: light microscopy, electron microscopy, and immunofluorescence. For the initial biopsy, all methods should be used; for subsequent biopsies, electron and immunofluorescent microscopy are performed only if indicated. This approach allows the pathologist to obtain maximal diagnostic and prognostic information. In selected instances, rapid processing or frozen sections can be performed on the tissue placed in fixative for light microscopy when an immediate assessment of the changes in the graft is necessary for initiating or modifying therapy.

Transplant Rejection

Traditionally, three major forms of rejection are recognized: hyperacute, acute, and chronic. Each has reasonably distinctive changes, although acute and chronic rejection may be present simultaneously, resulting in a mixture of histopathologic features. Pathologic findings in the major lesions responsible for functional impairment of the graft are shown in Table 13.2

Hyperacute Rejection

Hyperacute rejection is produced by preformed cytotoxic antibodies and is an infrequent event so long as the pretransplantation crossmatch is negative (see Chapters 3 and 5). It may manifest shortly after vascular anastomoses are established or may be delayed up to 2 to 3 days. It is characterized by rapid and widespread vascular thrombosis, predominantly affecting arteries, arterioles, and glomeruli, often with polymorphonuclear leukocytes incorporated in the thrombi. The kidney is usually cyanotic, slightly edematous, and flaccid, and urine production suddenly ceases or does not begin at all. If the kidney is not removed immediately, extensive cellular necrosis ensues, followed after 24 hours by numerous cortical and medullary infarcts. Immunofluorescence may disclose capillary and arterial wall immunoglobulin G (IgG) or IgM, C3, and fibrin, with fibrin also in the thrombi. Electron microscopy in the early lesions indicates degeneration and early necrosis of vascular endothelium.

Table 13.2. Histopathologic findings in the major causes of allograft dysfunction

Type	Interstitium	Tubules	Glomeruli	Arteries
Acute cellular rejection	Edema, lymphocytes	Lymphocytes, cell degeneration	Capillary lymphocytes	Swollen endothelium, lymphocytes, foam cells
Acute humoral rejection	Hemorrhage, zonal necrosis (infarction)	Necrosis	Neutrophils, thrombosis	Necrosis, neutrophils, thrombosis
Acute tubular necrosis	Edema	Cell degeneration, necrosis, mitotic figures	Normal	Normal
Acute cyclosporine toxicity	Edema	Isometric vacuoles	Normal	Normal
Chronic rejection	Fibrosis, lymphocytes	Atrophy, drop-out	Chronic transplant glomerulopathy	Fibrosis, lymphocytes, narrowed lumina
Chronic cyclosporine toxicity	"Striped" fibrosis	Atrophy	Ischemic collapse	Arteriopathy, hyalinization

necessary to have a dedicated social worker or pharmacist available to help patients find ways to cover the cost of their immunosuppressive medications.

6. Identify patients who are at high risk for noncompliance. Adolescent patients are at increased risk, often because they are fearful of the cosmetic effects of prednisone and cyclosporine. Patients who are poorly educated are also at increased risk for noncompliance. Similarly, low family income is associated with noncompliance. Socioeconomic factors place members of racial minorities at increased risk for noncompliance. Studies have shown that patients who were noncompliant with medication, diet, and dialysis therapy before transplantation are more likely to be noncompliant after renal transplantation.
7. Patients who are at high risk for noncompliance should be targeted with risk factor intervention in much the same way that we target patients who are at high risk for cardiovascular disease with intensive risk factor management. In both instances, the benefit is likely to be the greatest when the risk is the highest.

Strategy 3: Monitor Renal Function Closely

Frequent monitoring of renal function in the late posttransplantation period helps to enforce compliance with immunosuppressive medications and provides the only reliable means to detect acute rejection when it may still respond to treatment. A program requiring patients to make certain that serum creatinine is measured regularly and reported to the transplantation center also provides an indirect means for the center to monitor compliance. Patients who fail to have their serum creatinine level checked regularly should be contacted and reminded of the importance of close, ongoing follow-up to prevent graft failure. Patients and caregivers should be constantly reminded that acute rejection rarely presents with signs and symptoms in the late posttransplantation period. Serum creatinine levels can be measured in most laboratories relatively inexpensively. This test is the only practical tool that can be used to screen for acute rejection in the late posttransplantation period. It is not too much to ask patients to have their serum creatinine level measured regularly in the late posttransplantation period.

At least once a year, and preferably more often, urine should be checked for protein excretion. Persistent proteinuria (i.e., more than 1 g in 24 hours for at least 6 months) is associated with an increased risk for graft failure. Proteinuria can be most reliably detected by either a timed urine collection (which is cumbersome) or a protein-to-creatinine ratio measured in a random "spot" urine sample (which is convenient). Dipstick screening is less reliable because the protein concentration is also dependent on the state of diuresis. There are two reasons why it is important to detect proteinuria:

1. Reducing high levels of proteinuria with angiotensin-converting enzyme (ACE) inhibitors or receptor antagonists may help reduce levels of serum cholesterol and alleviate coagulation and other metabolic abnormalities associated with nephrotic-range proteinuria.

2. There is growing circumstantial evidence that proteinuria may itself be injurious to the kidney and may contribute to the pathogenesis of chronic allograft nephropathy.

Strategy 4: Perform Biopsy to Detect Late Acute Rejection

There is evidence to suggest that even low-grade tubulitis, or *borderline acute rejection*, may increase the risk for chronic allograft nephropathy. A small, randomized, controlled trial has demonstrated that treating acute rejection on protocol biopsies during the first few months after transplantation resulted in a lower serum creatinine level at 2 years, as compared with controls who underwent less frequent biopsies and relied instead on increased serum creatinine levels to prompt biopsy and treatment (see Chapter 8). Few centers perform protocol biopsies, that is, biopsies on all patients at predetermined intervals, in the late posttransplantation period. However, the message is clear. It is important to have a high level of suspicion for acute rejection and a low threshold for obtaining a renal allograft biopsy. An acute, sustained rise in serum creatinine should prompt immediate evaluation. The strategy of routinely monitoring serum creatinine levels (described previously) will only be successful if biopsies are obtained quickly and acute rejection is treated. Such a strategy will also avoid unnecessary intensification of immunosuppression when rejection is not present. After chronic allograft nephropathy is established, repeated biopsies may be unnecessary because repeated treatment may be unwise (see Chapter 4).

Strategy 5: Treat Hyperlipidemia Aggressively

Hyperlipidemia is common after renal transplantation. Elevations in total cholesterol are almost invariably accompanied by elevations in LDL cholesterol. Triglycerides are also frequently elevated. Several studies have found correlations between hyperlipidemia and cardiovascular disease after renal transplantation. Studies in the general population have provided incontrovertible evidence that treatment of elevated LDL reduces the risk for ischemic heart disease events and decreases mortality. Because an increased LDL level is the most common lipid abnormality after renal transplantation, it is reasonable to follow the National Cholesterol Education Program (NCEP) guidelines for treatment (Table 9.9). A National Kidney Foundation task force on CVD reached the same conclusion, but went further to suggest that transplant recipients should be considered in the highest risk category when applying the NCEP guidelines. Accordingly, transplant recipients with LDL cholesterol levels of more than 130 mg/dL should be considered for pharmacologic treatment, especially if they have preexisting CVD, diabetes, or other risk factors.

Reduction of the urine protein excretion with an ACE inhibitor or receptor antagonist may help to reduce lipid levels for patients with nephrotic-range proteinuria. Reduction or discontinuation of cyclosporine, sirolimus, or prednisone may also help lower lipid levels. Diet is effective in reducing cholesterol and LDL, but the effect is usually modest. A number of studies have shown that HMG-CoA reductase inhibitors are safe and effective in lowering LDL cholesterol after renal transplantation. Plasma levels of

may represent laboratory variability, and recognition of their significance is sometimes more of an art form than a science! If there is any question regarding a small asymptomatic rise in the plasma creatinine concentration, the test should be repeated within 48 hours, and the directional change usually facilitates its clinical evaluation.

Anatomic or surgical problems must be excluded before "medical" diagnoses are made to explain deteriorating graft function. Doppler ultrasound is invaluable (see Chapter 12), and it should be performed before any major therapeutic intervention. Scintigraphic scans are nonspecific in the setting of ATN, rejection, or drug toxicity and are of limited diagnostic value at this stage.

The gold-standard diagnostic tool is either the kidney biopsy or fine-needle aspiration biopsy (see Chapter 13). The timing and frequency of kidney biopsies vary between centers. One clinical approach to graft dysfunction is to make a therapeutic intervention empirically based on the clinical presentation and laboratory values. A favorable response confirms the diagnosis, but a lack of a response likely requires a tissue diagnosis. A tissue diagnosis of rejection should always precede a course of OKT3 or polyclonal antibodies. This policy is wise because unanticipated diagnoses, such as nephrotoxicity, CMV infection, posttransplantation lymphoma, or polyomavirus infection, may be made, and such findings require reduction of immunosuppression rather than intensification.

A more precise and increasingly routine approach to graft dysfunction is to perform a kidney biopsy whenever the serum creatinine level increases over the baseline value.

A 25% increase is usually enough to trigger a response that recognizes the observation that clinical diagnosis of graft dysfunction is unreliable. Therapy is then based on the histologic findings. In each transplantation center, a protocol should be developed that logically incorporates both noninvasive and invasive techniques to evaluate allograft dysfunction during this time period.

Protocol Biopsies

Up to 30% of clinically stable patients may experience subclinical rejection episodes that do not produce overt renal dysfunction or elevation in serum creatinine values. Subclinical rejections are typically mild by pathologic criteria (Banff type 1; see Chapter 13). Recognition of subclinical rejection requires uniform performance of protocol biopsies at prespecified posttransplantation intervals. The approach to treatment and the long-term effect of these episodes are unresolved, although a prospective study has shown that treatment with corticosteroids may lead to a reduction in the incidence of clinical rejections and improvement in long-term function and histology. Protocol biopsies performed for clinical purposes have not yet become standard practice in most transplantation centers, although they represent a potentially valuable approach to management.

Calcineurin Inhibitor Levels

Despite nearly two decades of experience with cyclosporine and a decade of experience with tacrolimus, there remains a lack of uni-

formity regarding the use of trough blood levels in routine patient management. Guidelines for dosage are provided in Chapter 4. It is clear that high blood levels of these agents do not preclude a diagnosis of rejection and that nephrotoxicity may occur at apparently low levels. Nephrotoxicity and rejection may coexist. With these provisos, however, it is fair to presume initially that a patient with deteriorating graft function and a very high cyclosporine or tacrolimus level is probably suffering from nephrotoxicity and that a patient with deteriorating graft function and very low levels is probably undergoing acute rejection. If the appropriate clinical therapeutic response does not have a salutary effect on graft function, the clinical premise needs to be reconsidered. Acute calcineurin inhibitor toxicity usually resolves within 24 to 48 hours of a dose reduction. Progressive elevation of the plasma creatinine level, even in the face of persistently high drug levels, is highly suggestive of rejection. Acute rejection may present as dramatic deterioration of graft function, whereas it is unusual for calcineurin inhibitor toxicity to produce a greater than 50% elevation of the plasma creatinine level.

Graft Tenderness

Graft tenderness on palpation in the first few days after transplantation is usually an innocuous finding related to recent surgery. In a stable patient, it is important to palpate the graft regularly to provide a clinical baseline for future changes. The development of graft tenderness in a previously pain-free, stable patient is a significant symptom that needs to be evaluated. A tender, swollen graft in a patient with a rising creatinine concentration and fever usually indicates rejection, although the possibility of acute pyelonephritis must be considered. Calcineurin inhibitor toxicity and CMV infection do not produce graft tenderness. Excruciating localized perinephric pain is usually due to a urine leak.

Fluid Retention and Oliguria

Both rejection and cyclosporine toxicity may produce weight gain and edema due to impaired GFR and avid tubular sodium reabsorption. Mild peripheral edema is common in stable patients receiving cyclosporine and usually responds to oral furosemide. Both acute rejection and calcineurin inhibitor toxicity can produce graft dysfunction in the absence of oliguria. Oliguria is common in acute rejection but makes a diagnosis of drug toxicity unlikely.

Common Laboratory Abnormalities

Urinalysis

Examination of the urine for the presence of red and white blood cells, bacteria, and protein should be part of the routine outpatient visit. Pyuria can indicate either rejection or infection, and the urine should be cultured. The presence of proteinuria may herald the early recurrence of the primary kidney disease or chronic rejection; in the case of patients at risk for recurrent focal sclerosis, the finding of proteinuria is an indication for graft biopsy because plasmapheresis may be indicated (see Chapter 9). Trace or "one plus" proteinuria, amounting to less than 500 mg/day,

Reproducibility of the Banff schema in reporting protocol biopsies of stable renal allografts.

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BACKGROUND: There is evidence that biopsy of stable renal allografts may be of value in predicting chronic allograft nephropathy, the main cause of graft loss. However, the reproducibility of such histological evaluation has not been tested in this setting. We tested the reproducibility of the Banff schema for this purpose. **METHODS:** We rated acute and chronic changes in 184 protocol biopsies. Individual pathologists at two different Canadian transplant centres reported independently. **RESULTS:** There was agreement in 73.53, 42.86, and 77.08% of cases in assigning a diagnosis of acute rejection, borderline changes (as defined in the schema), and no acute rejection, respectively. Applying kappa statistics, there was very good agreement in making the diagnosis of acute rejection vs no acute rejection (kappa 0.77). There was good inter-observer agreement in scoring glomerulitis, intimal arteritis, interstitial infiltrates, tubulitis, and arteriolar hyalinosis. Rating chronic changes also gave good inter-observer agreement (kappa=0.53, 0.65, and 0.62, respectively, for mild, moderate, and severe chronic allograft nephropathy). Agreement on transplant glomerulopathy was, however, poor. **CONCLUSIONS:** We conclude that the Banff classification provides a reproducible method for the histological assessment of protocol renal allograft biopsies in stable grafts. Such biopsies may be valuable in detecting subclinical rejection and early chronic allograft nephropathy and may also be used as surrogate end-points in the evaluation of therapy to prevent the latter.

Semin Nephrol 2002 May;22(3):254-67

Percutaneous renal biopsy.

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Percutaneous renal biopsy (PRB) is an integral part of the clinical practice of nephrology. It is essential in the diagnosis of glomerular, vascular, and tubulointerstitial diseases of the kidney, providing information that is invaluable in prognosis and patient management. The use of real-time ultrasound and automated biopsy needles has simplified and improved the success and safety of this procedure. In the recent past, we have seen a shift of the PRB from nephrologists to radiologists and this has raised appropriate concern that loss of this procedure may undermine the nephrologist's status as a subspecialist. We must continue to properly train young nephrologists in the proper technique and value of performing renal biopsy procedures or we stand to lose control of a procedure that was an integral part of the development of our subspecialty. Copyright 2002, Elsevier Science.

2.5 WP

analysed with Analyse-It + Clinical Laboratory 1 62

Test Receiver Operator Characteristic (ROC) curves

M2570_53 by SAMP_GRP

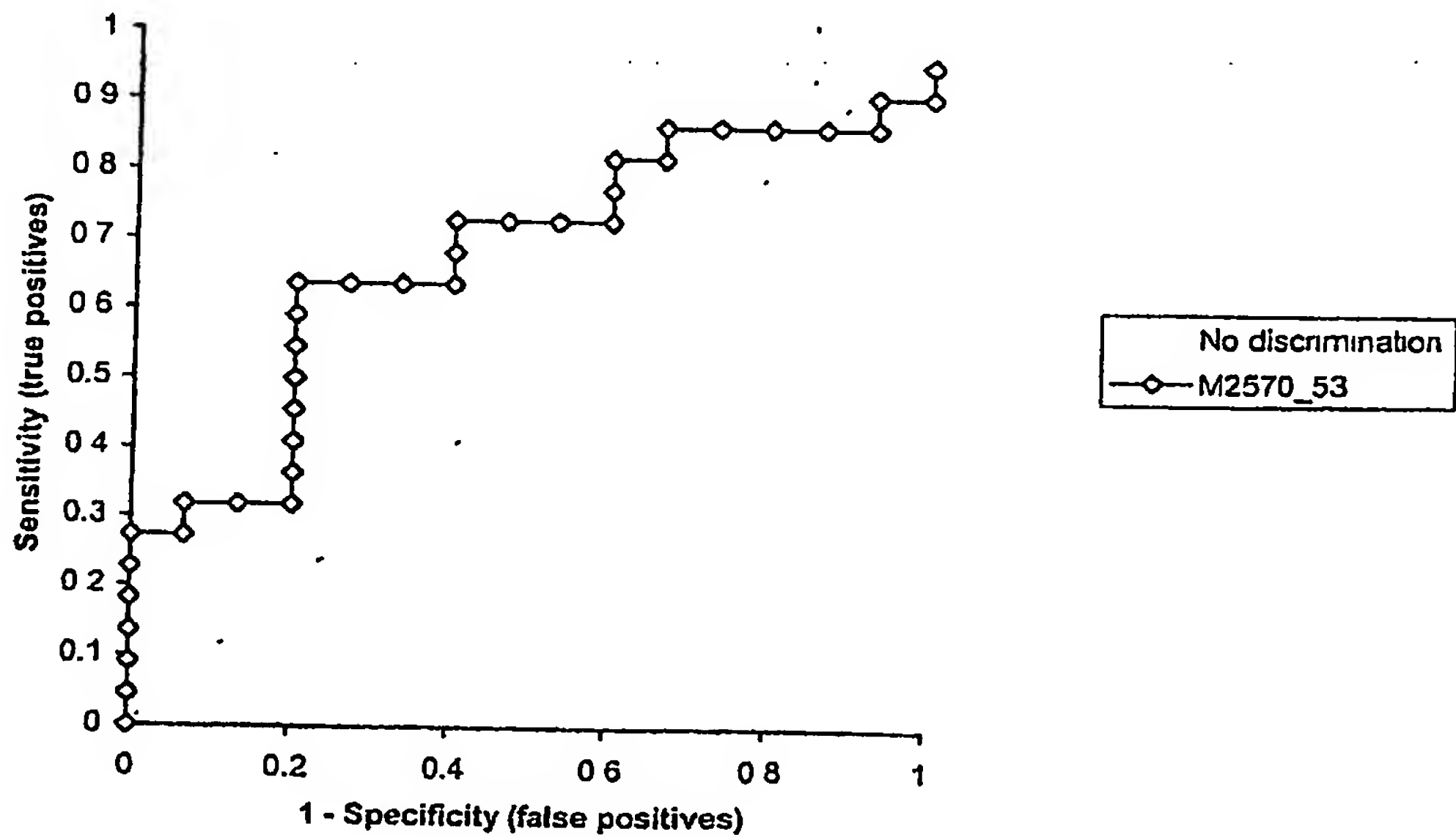
Performed by

Date

n | 37

SAMP_GRP	n
0	15
1	22

Curve	Area	SE	p	95% CI of Area	SAMP_GRP = 1
M2570_53	0.679	0.0893	0.0226	0.504 to 0.854	have higher values



M2570_53 (abnormals above cut-off)	Sensitivity	Specificity	TP	TN	FP	FN
-2.269465893	95.5%	0.0%	21	0	15	1

Test Receiver Operator Characteristic (ROC) curves

M2570_53 by SAMP_GRP

Performed by					Date	
-1.951002658	90 9%	0 0%	20	0	15	2
-1.83330003	90.9%	6.7%	20	1	14	2
-1.269532325	86 4%	6.7%	19	1	14	3
-0.749250767	86.4%	13.3%	19	2	13	3
-0.686191804	86.4%	20.0%	19	3	12	3
-0.480561789	86 4%	26.7%	19	4	11	3
-0.24696523	86.4%	33.3%	19	5	10	3
-0.164089193	81.8%	33.3%	18	5	10	4
2.081687311	81 8%	40 0%	18	6	9	4
3.295632696	77.3%	40.0%	17	6	9	5
3.365034205	72.7%	40.0%	16	6	9	6
3.59872779	72.7%	46.7%	16	7	8	6
3.616006133	72 7%	53 3%	16	8	7	6
3.817845849	72.7%	60.0%	16	9	6	6
3.83625841	68 2%	60.0%	15	9	6	7
3.939338679	63.6%	60.0%	14	9	6	8
4.158036338	63 6%	66.7%	14	10	5	8
4.708928058	63.6%	73.3%	14	11	4	8
4.720146774	63.6%	80.0%	14	12	3	8
4.848737034	59.1%	80.0%	13	12	3	9
4.883287628	54 5%	80.0%	12	12	3	10
5.58382828	50.0%	80 0%	11	12	3	11
5.63657289	45.5%	80.0%	10	12	3	12
5.97481079	40 9%	80 0%	9	12	3	13
6.303358832	36.4%	80.0%	8	12	3	14
7.678719546	31.8%	80.0%	7	12	3	15
8.0975886	31.8%	86.7%	7	13	2	15
8.927745106	31.8%	93.3%	7	14	1	15
9.115824471	27.3%	93 3%	6	14	1	16
9.841141821	27 3%	100 0%	6	15	0	16
9.880647941	22.7%	100 0%	5	15	0	17
10.02241699	18.2%	100.0%	4	15	0	18
10.07505391	13.6%	100.0%	3	15	0	19
10.65260521	9.1%	100.0%	2	15	0	20
16.80229123	4 5%	100.0%	1	15	0	21
102.3283407	0.0%	100.0%	0	15	0	22

2.6 WD

analysed with Analyse-IT + Clinical Laboratory 1.62

Test Receiver Operator Characteristic (ROC) curves

M2606_59 by SAMP_GRP

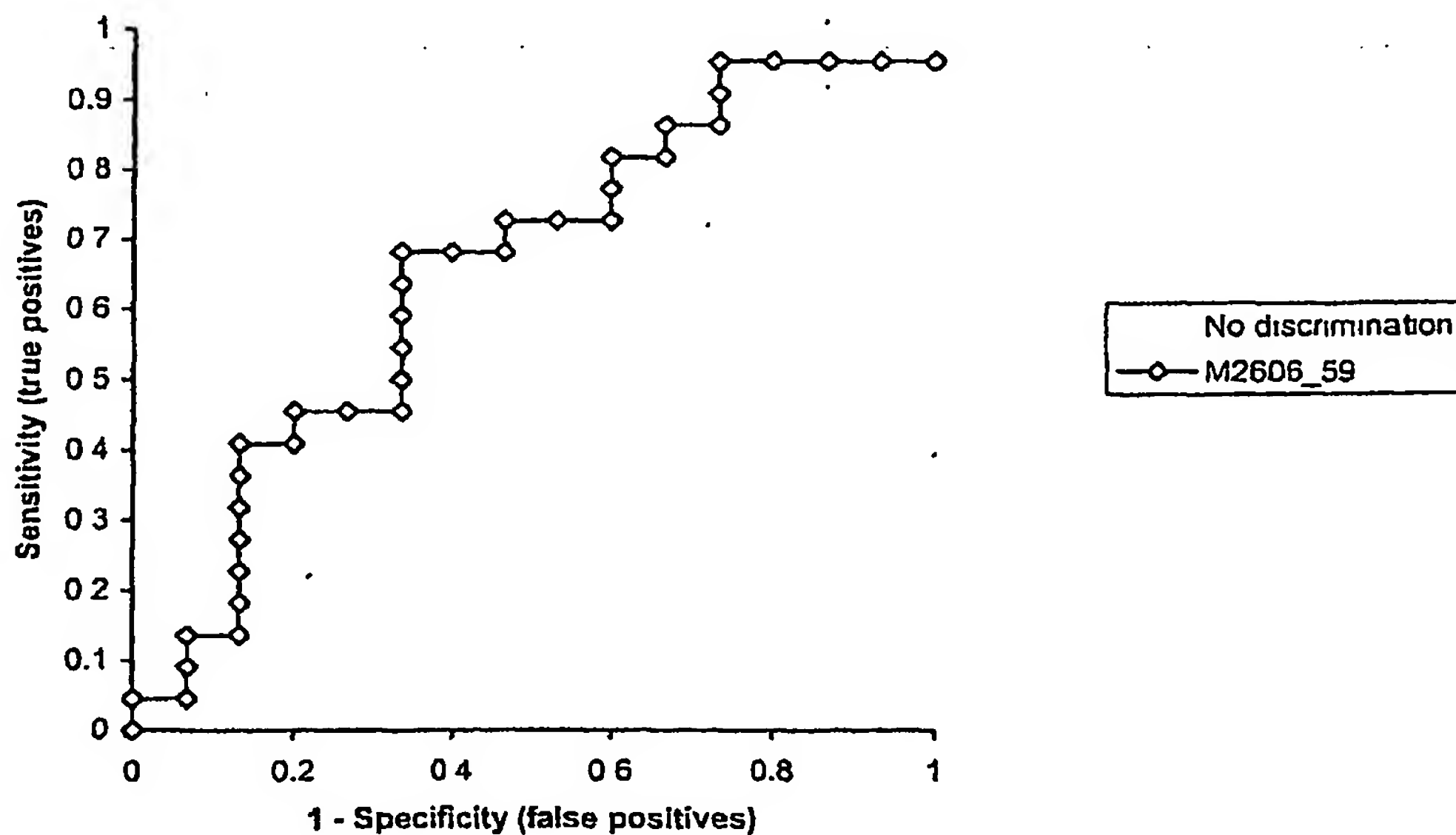
Performed by

Date

n 37

SAMP_GRP	n
0	15
1	22

Curve	Area	SE	p	95% CI of Area	SAMP_GRP = 1
M2606_59	0.655	0.0941	0.0502	0.470 to 0.839	have higher values



M2606_59 (abnormals above cut-off)	Sensitivity	Specificity	TP	TN	FP	FN
-1.080932112	95.5%	0.0%	21	0	15	1

analysed with Analyse-It + Clinical Laboratory 1 62

Test Receiver Operator Characteristic (ROC) curves

M2606_59 by SAMP_GRP

Performed by					Date	
0.027827364	95.5%	6.7%	21	1	14	1
0.683141072	95.5%	13.3%	21	2	13	1
1.149352525	95.5%	20.0%	21	3	12	1
2.01440388	95.5%	26.7%	21	4	11	1
2.950097316	90.9%	26.7%	20	4	11	2
3.291169441	86.4%	26.7%	19	4	11	3
3.426174559	86.4%	33.3%	19	5	10	3
5.038025584	81.8%	33.3%	18	5	10	4
5.08703796	81.8%	40.0%	18	6	9	4
5.543285249	77.3%	40.0%	17	6	9	5
6.109528354	72.7%	40.0%	16	6	9	6
6.138626935	72.7%	46.7%	16	7	8	6
7.607489067	72.7%	53.3%	16	8	7	6
7.910857563	68.2%	53.3%	15	8	7	7
8.75882275	68.2%	60.0%	15	9	6	7
8.819047007	68.2%	66.7%	15	10	5	7
8.980914241	63.6%	66.7%	14	10	5	8
9.709094998	59.1%	66.7%	13	10	5	9
10.08745897	54.5%	66.7%	12	10	5	10
11.04608025	50.0%	66.7%	11	10	5	11
11.63267593	45.5%	66.7%	10	10	5	12
12.49374817	45.5%	73.3%	10	11	4	12
12.60732604	45.5%	80.0%	10	12	3	12
13.50273042	40.9%	80.0%	9	12	3	13
13.82143605	40.9%	86.7%	9	13	2	13
16.7254242	36.4%	86.7%	8	13	2	14
17.41424302	31.8%	86.7%	7	13	2	15
18.06049443	27.3%	86.7%	6	13	2	16
18.20894302	22.7%	86.7%	5	13	2	17
23.27328015	18.2%	86.7%	4	13	2	18
24.08280508	13.6%	86.7%	3	13	2	19
25.98483956	13.6%	93.3%	3	14	1	19
26.57746175	9.1%	93.3%	2	14	1	20
28.83048001	4.5%	93.3%	1	14	1	21
47.62329377	4.5%	100.0%	1	15	0	21
166.8780076	0.0%	100.0%	0	15	0	22

3.42

Test Receiver Operator Characteristic (ROC) curves

M3388_17 by SAMP_GRP

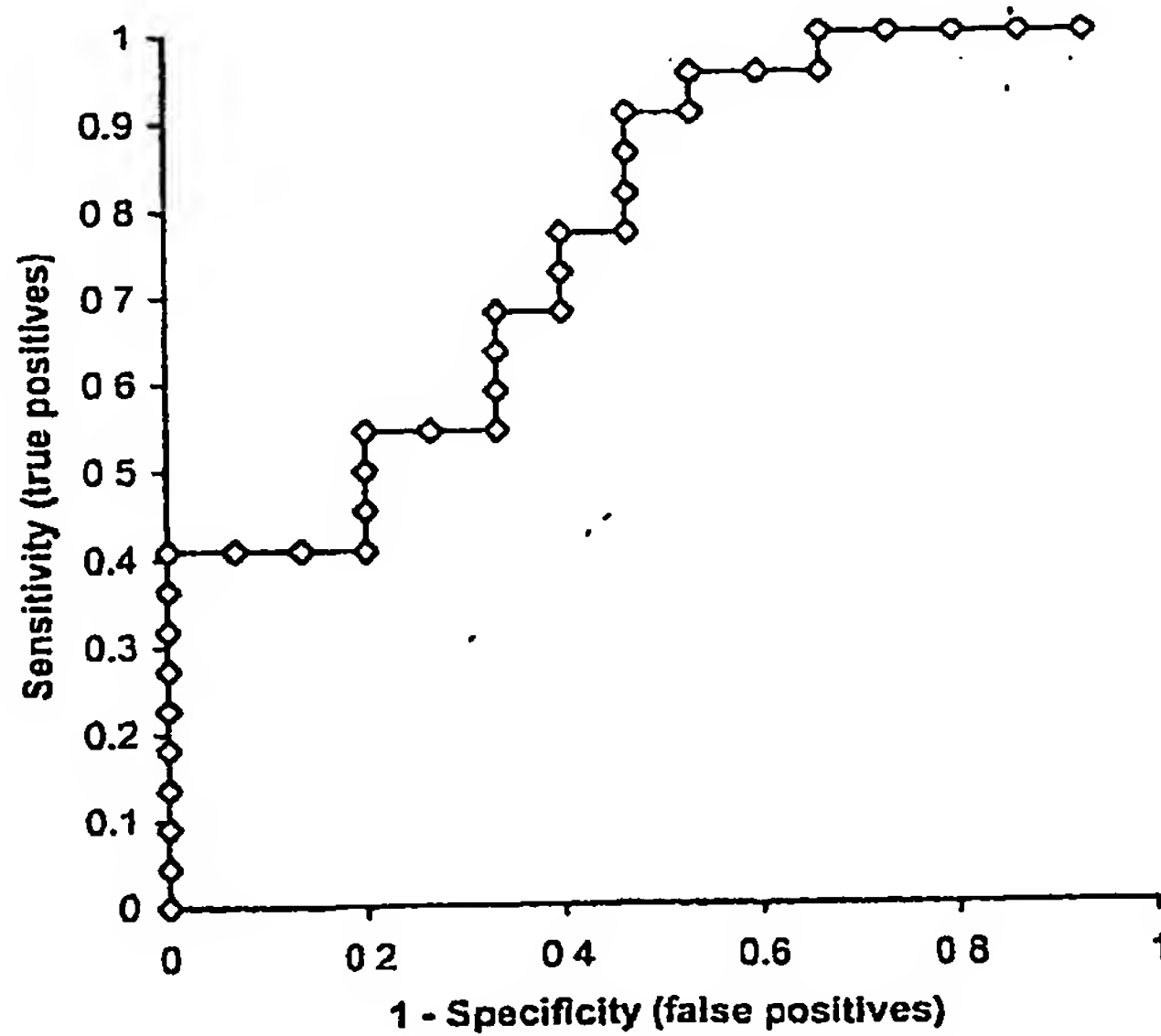
Performed by

Date

n | 37

SAMP_GRP	n
0	15
1	22

Curve	Area	SE	p	95% CI of Area	SAMP_GRP = 1
M3388_17	0.773	0.0782	0.0002	0.620 to 0.926	have higher values



M3388_17 (abnormals above cut-off)	Sensitivity	Specificity	TP	TN	FP	FN
6.069828529	100.0%	6.7%	22	1	14	0

Test Receiver Operator Characteristic (ROC) curves

M3388_17 by SAMP_GRP

Performed by					Date	
7.207024304	100.0%	13.3%	22	2	13	0
9.922083432	100.0%	20.0%	22	3	12	0
10.17708081	100.0%	26.7%	22	4	11	0
10.56576285	100.0%	33.3%	22	5	10	0
10.59455925	95.5%	33.3%	21	5	10	1
10.91545247	95.5%	40.0%	21	6	9	1
12.29222011	95.5%	46.7%	21	7	8	1
13.37211543	90.9%	46.7%	20	7	8	2
13.55951694	90.9%	53.3%	20	8	7	2
13.91148758	86.4%	53.3%	19	8	7	3
15.27682835	81.8%	53.3%	18	8	7	4
17.64519175	77.3%	53.3%	17	8	7	5
19.34493728	77.3%	60.0%	17	9	6	5
21.08732753	72.7%	60.0%	16	9	6	6
22.76287936	68.2%	60.0%	15	9	6	7
25.28009079	68.2%	66.7%	15	10	5	7
28.47442488	63.6%	66.7%	14	10	5	8
29.29347057	59.1%	66.7%	13	10	5	9
32.64837117	54.5%	66.7%	12	10	5	10
33.79327766	54.5%	73.3%	12	11	4	10
34.64644181	54.5%	80.0%	12	12	3	10
35.2582956	50.0%	80.0%	11	12	3	11
43.35388576	45.5%	80.0%	10	12	3	12
44.33466793	40.9%	80.0%	9	12	3	13
57.15728342	40.9%	86.7%	9	13	2	13
57.34024544	40.9%	93.3%	9	14	1	13
58.57318233	40.9%	100.0%	9	15	0	13
67.95461705	36.4%	100.0%	8	15	0	14
73.51997985	31.8%	100.0%	7	15	0	15
81.8346206	27.3%	100.0%	6	15	0	16
84.87048686	22.7%	100.0%	5	15	0	17
95.23399501	18.2%	100.0%	4	15	0	18
111.3451323	13.6%	100.0%	3	15	0	19
135.2673113	9.1%	100.0%	2	15	0	20
163.0844717	4.5%	100.0%	1	15	0	21
244.1203177	0.0%	100.0%	0	15	0	22

3.5/10

Test Receiver Operator Characteristic (ROC) curves

analysed with Analyse-it + Clinical Laboratory 1 62

M3504_43 by SAMP_GRP

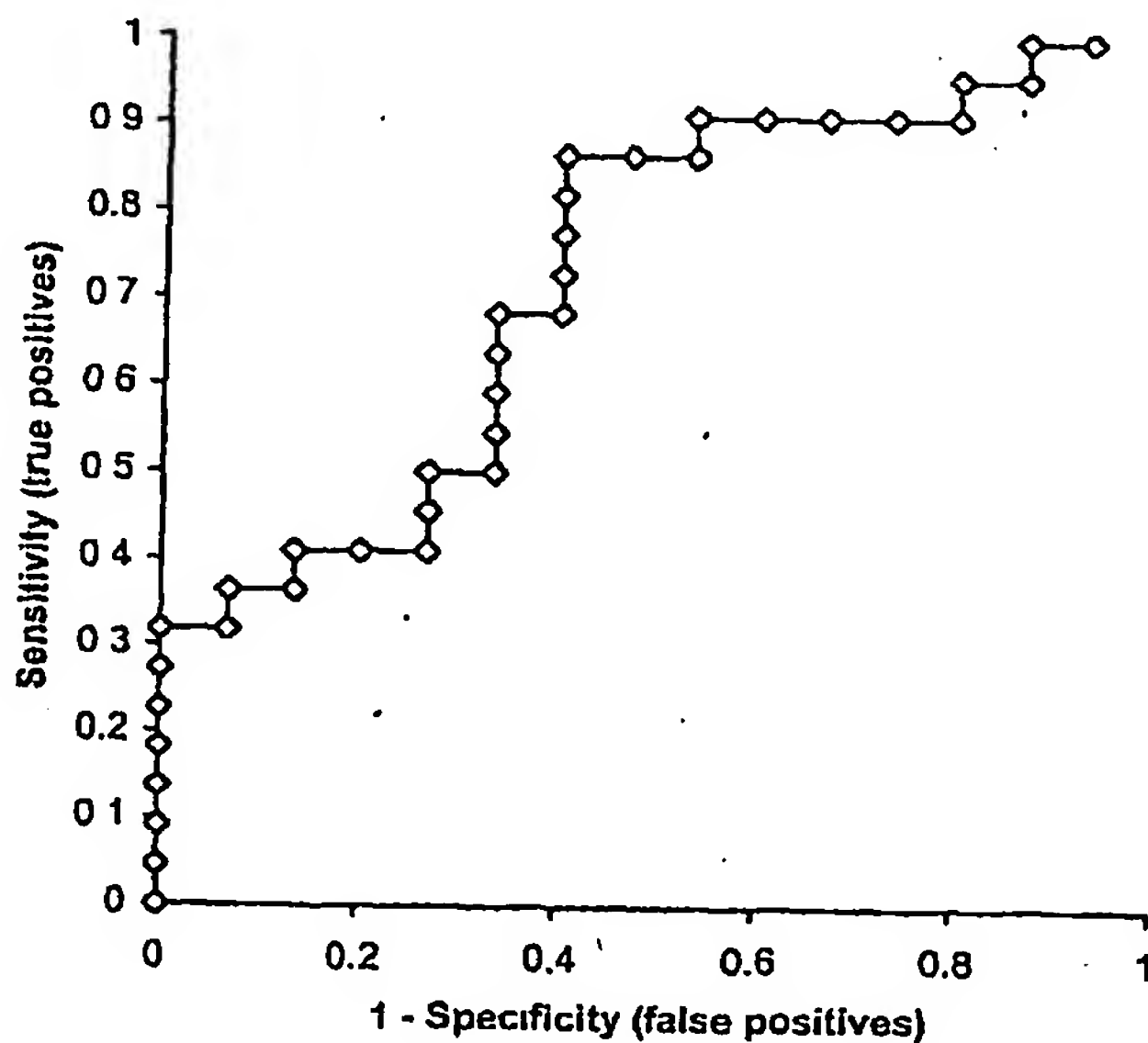
Performed by

Date

n | 37

SAMP_GRP	n
0	15
1	22

Curve	Area	SE	p	95% CI of Area	SAMP_GRP = 1
M3504_43	0.733	0.0845	0.0029	0.568 to 0.899	have higher values



M3504_43 (abnormals above cut-off)	Sensitivity	Specificity	TP	TN	FP	FN
2.065567969	100.0%	6.7%	22	1	14	0

Test Receiver Operator Characteristic (ROC) curves

M3504_43 by SAMP_GRP

Performed by					Date	
4.147177377	100 0%	13.3%	22	2	13	0
4.346483678	95.5%	13 3%	21	2	13	1
5.179027946	95.5%	20.0%	21	3	12	1
6.233060653	90.9%	20.0%	20	3	12	2
6.38602063	90 9%	26.7%	20	4	11	2
6.501021458	90.9%	33 3%	20	5	10	2
6.546230005	90.9%	40 0%	20	6	9	2
6.937741113	90.9%	46 7%	20	7	8	2
7.284313736	86.4%	46 7%	19	7	8	3
7.518206292	86.4%	53.3%	19	8	7	3
9.33476608	86.4%	60.0%	19	9	6	3
9.532246496	81.8%	60 0%	18	9	6	4
9.781221999	77 3%	60.0%	17	9	6	5
9.866035899	72 7%	60.0%	16	9	6	6
16.00820213	68.2%	60.0%	15	9	6	7
18.92475045	68 2%	66 7%	15	10	5	7
19.75003398	63.6%	66 7%	14	10	5	8
19.79855126	59.1%	66.7%	13	10	5	9
20.02273661	54.5%	66.7%	12	10	5	10
24.21285993	50 0%	66.7%	11	10	5	11
29.87738742	50 0%	73.3%	11	11	4	11
30.43190207	45.5%	73 3%	10	11	4	12
31.64180193	40 9%	73.3%	9	11	4	13
39.09458711	40 9%	80.0%	9	12	3	13
40.19759412	40.9%	86 7%	9	13	2	13
42.40377564	36.4%	86 7%	8	13	2	14
44.91866348	36 4%	93.3%	8	14	1	14
53.46082451	31 8%	93 3%	7	14	1	15
57.85160936	31 8%	100.0%	7	15	0	15
61.00249637	27.3%	100.0%	6	15	0	16
72.50725155	22 7%	100.0%	5	15	0	17
80.1429293	18.2%	100.0%	4	15	0	18
81.42966987	13.6%	100 0%	3	15	0	19
94.0633764	9 1%	100 0%	2	15	0	20
102.5370068	4 5%	100.0%	1	15	0	21
131.0417084	0.0%	100 0%	0	15	0	22

3.8 WD

analysed with Analyse-IT + Clinical Laboratory 1 62

Test Receiver Operator Characteristic (ROC) curves

M3752_32 by SAMP_GRP

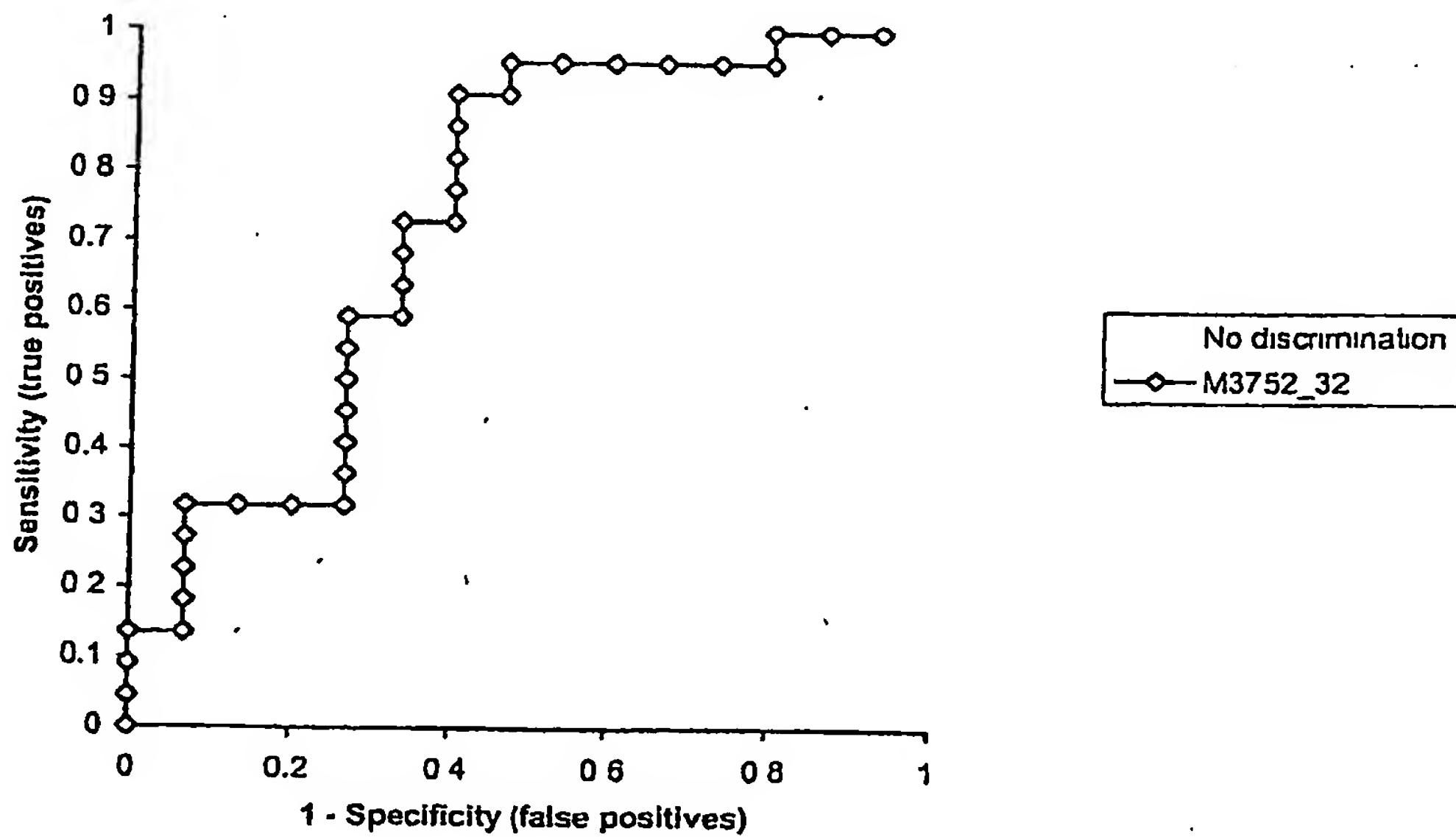
Performed by

Date

n | 37

SAMP_GRP	n
0	15
1	22

Curve	Area	SE	p	95% CI of Area	SAMP_GRP = 1
M3752_32	0.739	0.0892	0.0036	0.565 to 0.914	have higher values



M3752_32 (abnormals above cut-off)	Sensitivity	Specificity	TP	TN	FP	FN
0.714340764	100.0%	6.7%	22	1	14	0

U.S. DEPARTMENT OF AGRICULTURE

Test

M3752_32 by SAMP_GRP

Performed by _____

Date _____

U.1.122

Test Receiver Operator Characteristic (ROC) curves

analysed with Analyse-it + Clinical Laboratory 1

M4101_08 by SAMP_GRP

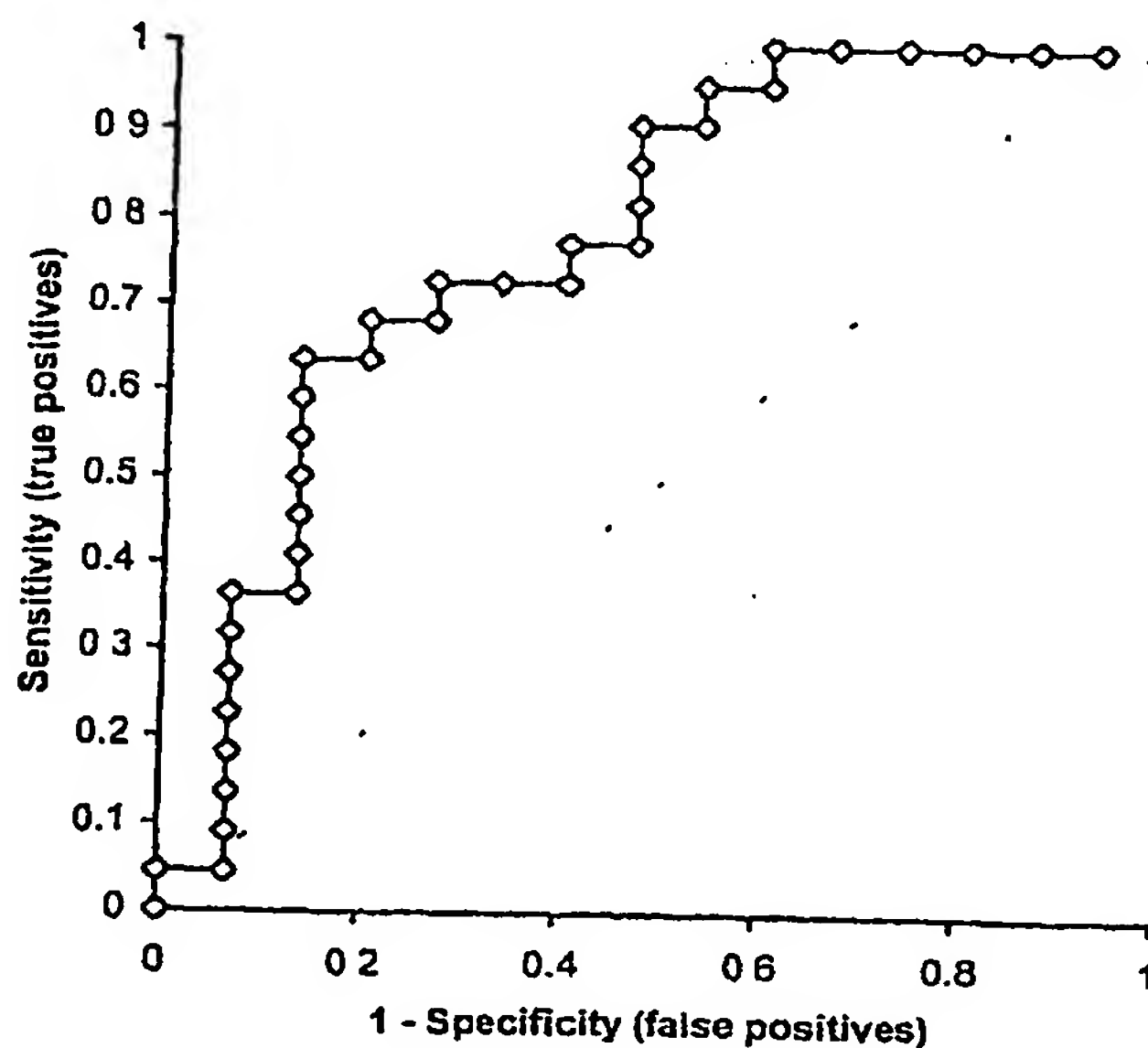
Performed by

Date

n | 37

SAMP_GRP	n
0	15
1	22

Curve	Area	SE	p	95% CI of Area	SAMP_GRP = 1
M4101_08	0.788	0.0806	0.0002	0.630 to 0.946	I have higher values



M4101_08 (abnormals above cut-off)	Sensitivity	Specificity	TP	TN	FP	FN
0.791227317	100.0%	6.7%	22	1	14	0

Test Receiver Operator Characteristic (ROC) curves

M4101_08 by SAMP_GRP

Performed by						Date	
1.777024145	100.0%	13.3%	22	2	13	0	
1.864611445	100.0%	20.0%	22	3	12	0	
2.229038148	100 0%	26.7%	22	4	11	0	
2.42141698	100.0%	33.3%	22	5	10	0	
2.565874221	100 0%	40 0%	22	6	9	0	
2.702019221	95.5%	40.0%	21	6	9	1	
2.843449311	95 5%	46.7%	21	7	8	1	
2.982981073	90.9%	46 7%	20	7	8	2	
3.090587735	90.9%	53.3%	20	8	7	2	
3.241431653	86.4%	53.3%	19	8	7	3	
3.60744697	81.8%	53.3%	18	8	7	4	
4.562443603	77.3%	53.3%	17	8	7	5	
4.903502945	77.3%	60.0%	17	9	6	5	
5.177222365	72.7%	60 0%	16	9	6	6	
5.181713211	72.7%	66.7%	16	10	5	6	
5.857837737	72 7%	73.3%	16	11	4	6	
6.977510421	68.2%	73.3%	15	11	4	7	
7.386528126	68.2%	80.0%	15	12	3	7	
8.779791432	63 6%	80.0%	14	12	3	8	
9.459555394	63.6%	86.7%	14	13	2	8	
10.7072921	59.1%	86.7%	13	13	2	9	
12.08088057	54 5%	86.7%	12	13	2	10	
14.15204918	50.0%	86.7%	11	13	2	11	
16.11396822	45 5%	86 7%	10	13	2	12	
17.28550508	40.9%	86.7%	9	13	2	13	
17.80691034	36.4%	86.7%	8	13	2	14	
18.43405031	36 4%	93 3%	8	14	1	14	
18.47433197	31.8%	93.3%	7	14	1	15	
22.34250211	27.3%	93.3%	6	14	1	16	
27.29265602	22 7%	93.3%	5	14	1	17	
28.67121222	18.2%	93.3%	4	14	1	18	
29.03664973	13.6%	93.3%	3	14	1	19	
36.20675533	9.1%	93.3%	2	14	1	20	
38.54127644	4.5%	93.3%	1	14	1	21	
43.59268294	4.5%	100.0%	1	15	0	21	
144.7568822	0.0%	100.0%	0	15	0	22	

4.7.2020

analysed with Analyse-it + Clinical Laboratory 1 62

Test Receiver Operator Characteristic (ROC) curves

M4740_77 by SAMP_GRP

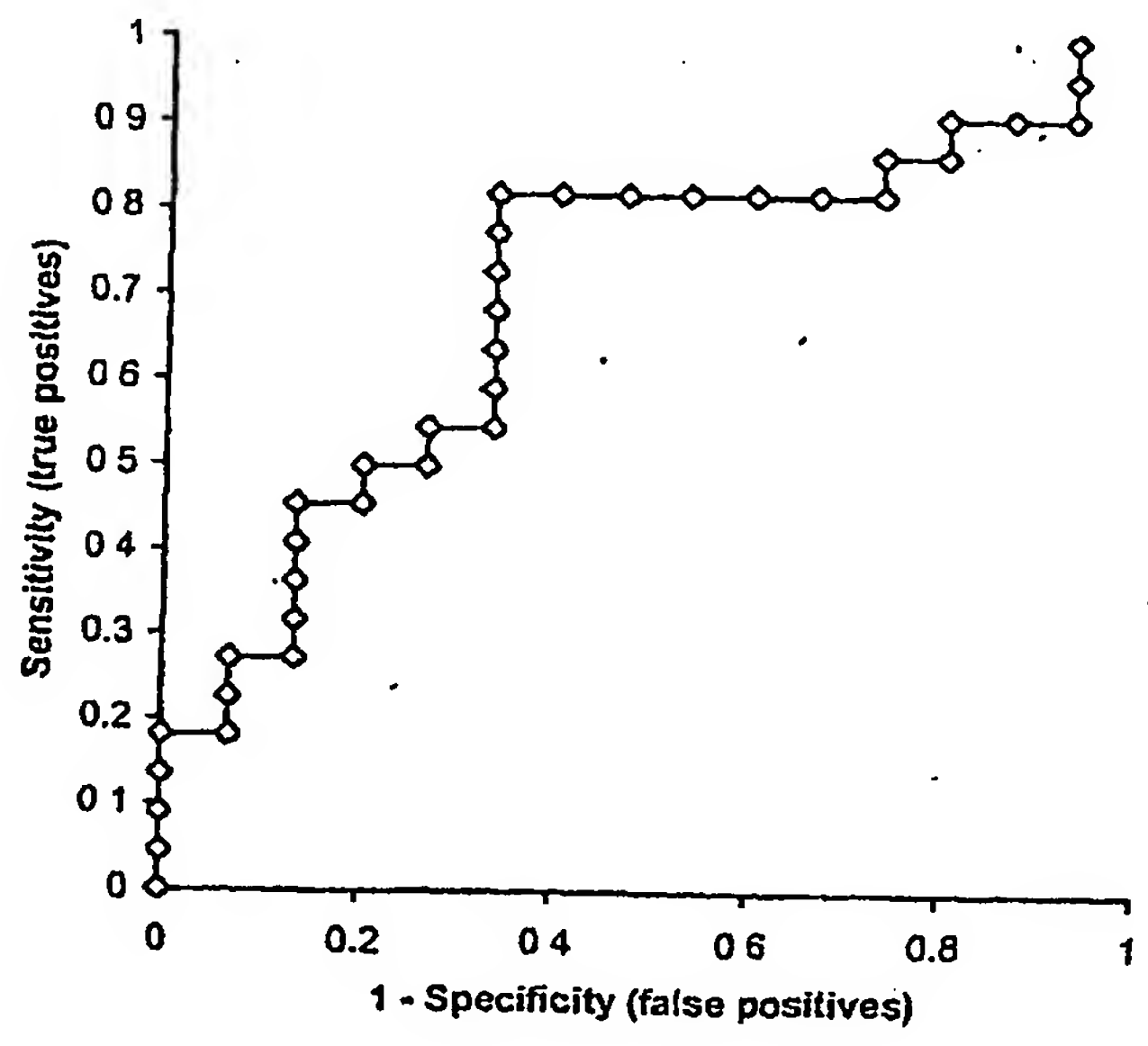
Performed by

Date

n | 37

SAMP_GRP	n
0	15
1	22

Curve	Area	SE	p	95% CI of Area	SAMP_GRP = 1
M4740_77	0.703	0.0885	0.0109	0.530 to 0.877	have lower values



M4740_77 (abnormals below cut-off)	Sensitivity	Specificity	TP	TN	FP	FN
1.782471733	0.0%	100.0%	0	15	0	22

Test Receiver Operator Characteristic (ROC) curves
M4740_77 by SAMP_GRP

Performed by					Date	
3.46751317	4 5%	100.0%	1	15	0	21
3.703141299	9.1%	100.0%	2	15	0	20
3.822882864	13 6%	100.0%	3	15	0	19
4.213531318	18.2%	100.0%	4	15	0	18
5.861586364	18.2%	93.3%	4	14	1	18
6.537592438	22.7%	93.3%	5	14	1	17
6.544283701	27.3%	93.3%	6	14	1	16
6.937836678	27.3%	86.7%	6	13	2	16
7.396949195	31.8%	86.7%	7	13	2	15
7.581156967	36 4%	86.7%	8	13	2	14
7.622572721	40.9%	86.7%	9	13	2	13
7.996831339	45.5%	86.7%	10	13	2	12
8.128229641	45 5%	80.0%	10	12	3	12
8.555890869	50.0%	80 0%	11	12	3	11
9.035229021	50.0%	73 3%	11	11	4	11
10.52413657	54.5%	73 3%	12	11	4	10
10.76436616	54 5%	66 7%	12	10	5	10
12.18334212	59.1%	66 7%	13	10	5	9
13.34623356	63 6%	66.7%	14	10	5	8
14.48398405	68.2%	66.7%	15	10	5	7
14.76122649	72.7%	66.7%	16	10	5	6
19.24801943	77.3%	66.7%	17	10	5	5
21.76687704	81 8%	66 7%	18	10	5	4
22.89440092	81.8%	60 0%	18	9	6	4
23.72554368	81.8%	53.3%	18	8	7	4
26.31956137	81.8%	46.7%	18	7	8	4
27.15591038	81.8%	40 0%	18	6	9	4
27.27126289	81 8%	33.3%	18	5	10	4
30.41172213	81.8%	26.7%	18	4	11	4
31.68687668	86.4%	26.7%	19	4	11	3
38.40570882	86.4%	20.0%	19	3	12	3
43.33855943	90.9%	20.0%	20	3	12	2
46.45290679	90.9%	13.3%	20	2	13	2
55.29038899	90.9%	6.7%	20	1	14	2
121.5530544	95.5%	6.7%	21	1	14	1
156.6316898	100 0%	6.7%	22	1	14	0

analysed with Analyse-It + Clinical Laboratory

4.8 WP

Test Receiver Operator Characteristic (ROC) curves

M4774_79 by SAMP_GRP

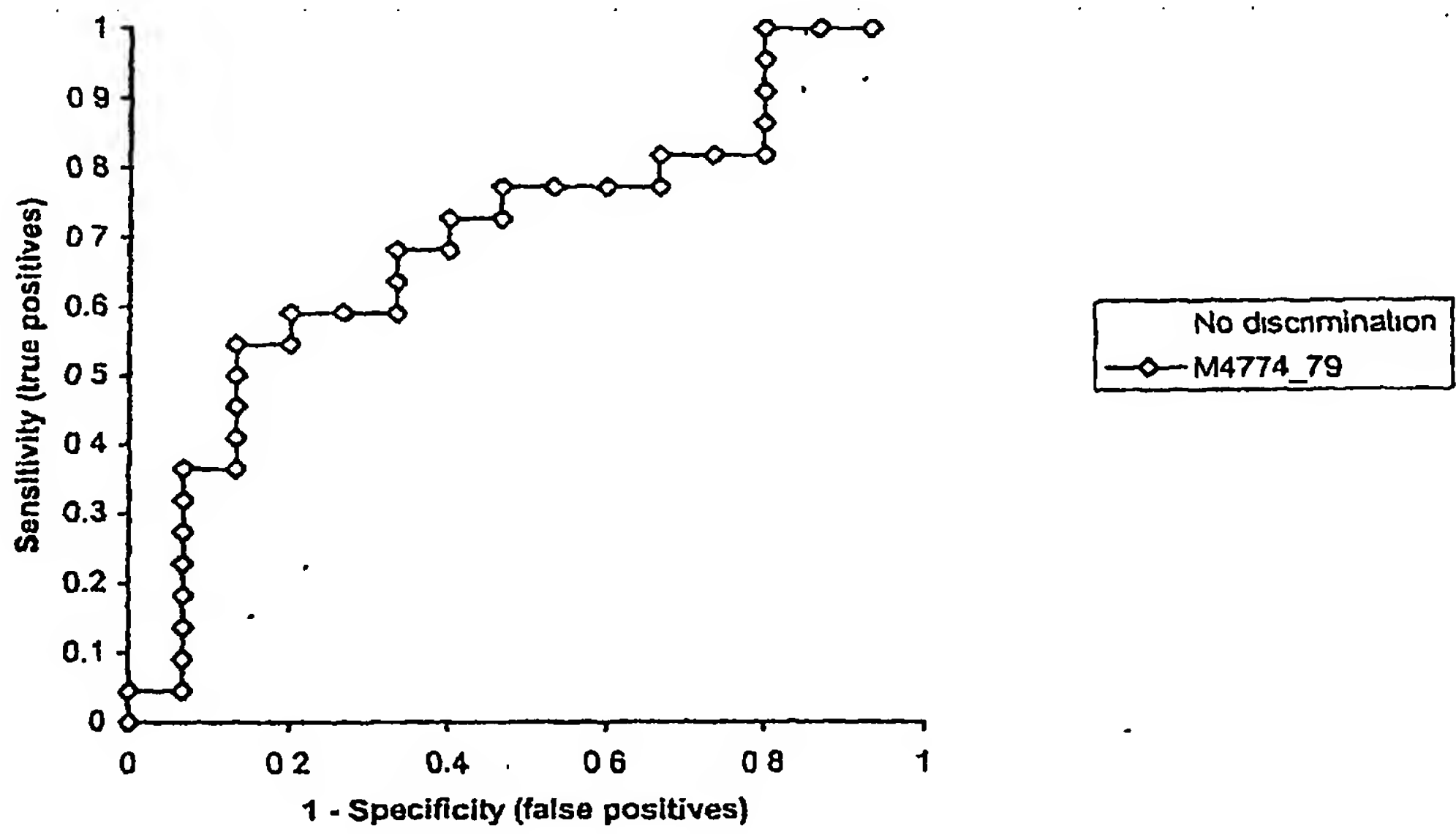
Performed by

Date

n | 37

SAMP_GRP	n
0	15
1	22

Curve	Area	SE	p	95% CI of Area	SAMP_GRP = 1
M4774_79	0.700	0.0888	0.0121	0.526 to 0.874	have lower values



M4774_79 (abnormals below cut-off)	Sensitivity	Specificity	TP	TN	FP	FN
1.628203756	0.0%	100.0%	0	15	0	22

Test Receiver Operator Characteristic (ROC) curves

M4774_79 by SAMP_GRP

Performed by					Date	
1.827155531	4.5%	100.0%	1	15	0	21
2.770794786	4.5%	93.3%	1	14	1	21
3.279957997	9.1%	93.3%	2	14	1	20
3.627411737	13.6%	93.3%	3	14	1	19
3.70851809	18.2%	93.3%	4	14	1	18
3.72785582	22.7%	93.3%	5	14	1	17
4.32411472	27.3%	93.3%	6	14	1	16
4.598018454	31.8%	93.3%	7	14	1	15
5.008617117	36.4%	93.3%	8	14	1	14
5.399934701	36.4%	86.7%	8	13	2	14
5.487403027	40.9%	86.7%	9	13	2	13
6.267387571	45.5%	86.7%	10	13	2	12
6.538557684	50.0%	86.7%	11	13	2	11
6.773605908	54.5%	86.7%	12	13	2	10
6.838166538	54.5%	80.0%	12	12	3	10
7.621667577	59.1%	80.0%	13	12	3	9
7.659773747	59.1%	73.3%	13	11	4	9
7.770546548	59.1%	66.7%	13	10	5	9
10.02116644	63.6%	66.7%	14	10	5	8
10.45039825	68.2%	66.7%	15	10	5	7
11.02281238	68.2%	60.0%	15	9	6	7
11.03992967	72.7%	60.0%	16	9	6	6
11.62998313	72.7%	53.3%	16	8	7	6
11.85826753	77.3%	53.3%	17	8	7	5
12.63500235	77.3%	46.7%	17	7	8	5
12.78702516	77.3%	40.0%	17	6	9	5
13.37119084	77.3%	33.3%	17	5	10	5
15.17345082	81.8%	33.3%	18	5	10	4
15.41808818	81.8%	26.7%	18	4	11	4
16.5708956	81.8%	20.0%	18	3	12	4
18.03957309	86.4%	20.0%	19	3	12	3
20.67017237	90.9%	20.0%	20	3	12	2
21.15863159	95.5%	20.0%	21	3	12	1
21.773702	100.0%	20.0%	22	3	12	0
23.69309466	100.0%	13.3%	22	2	13	0
37.43292643	100.0%	6.7%	22	1	14	0

SAMP

7. 8. 9. 10. 11. 12. 13. 14. 15. 16. 17. 18. 19. 20. 21. 22. 23. 24. 25. 26. 27. 28. 29. 30. 31. 32. 33. 34. 35. 36. 37. 38. 39. 40. 41. 42. 43. 44. 45. 46. 47. 48. 49. 50. 51. 52. 53. 54. 55. 56. 57. 58. 59. 60. 61. 62. 63. 64. 65. 66. 67. 68. 69. 70. 71. 72. 73. 74. 75. 76. 77. 78. 79. 80. 81. 82. 83. 84. 85. 86. 87. 88. 89. 90. 91. 92. 93. 94. 95. 96. 97. 98. 99. 100.

analysed with Analyse-it + Clinical Laboratory 1 62

Test Receiver Operator Characteristic (ROC) curves

M4991_74 by SAMP_GRP

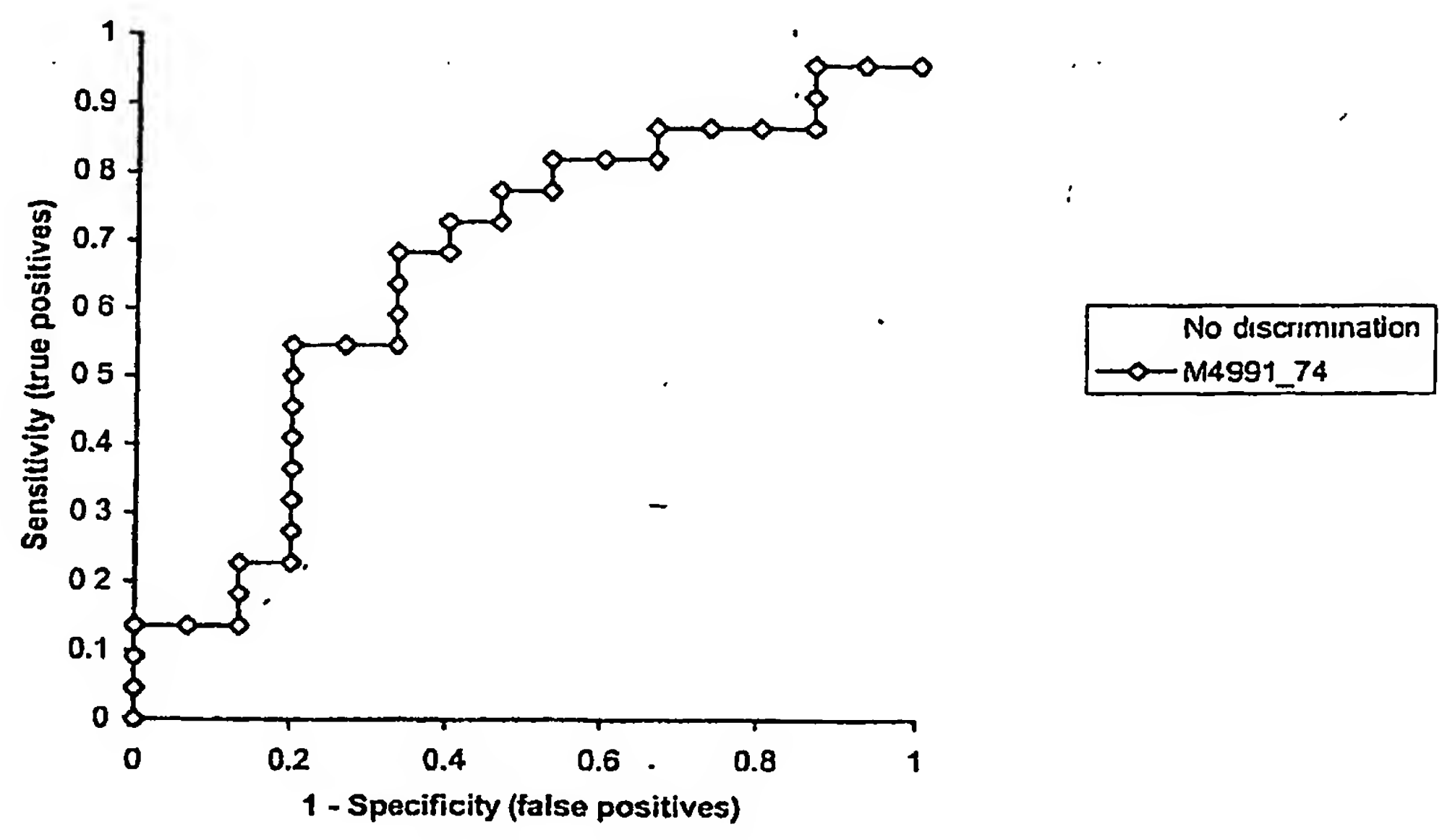
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|-------------------|
| M4991_74 | 0.661 | 0.0937 | 0.0433 | 0.477 to 0.844 | have lower values |



| M4991_74
(abnormals below cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| -0.196979745 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

515 MP

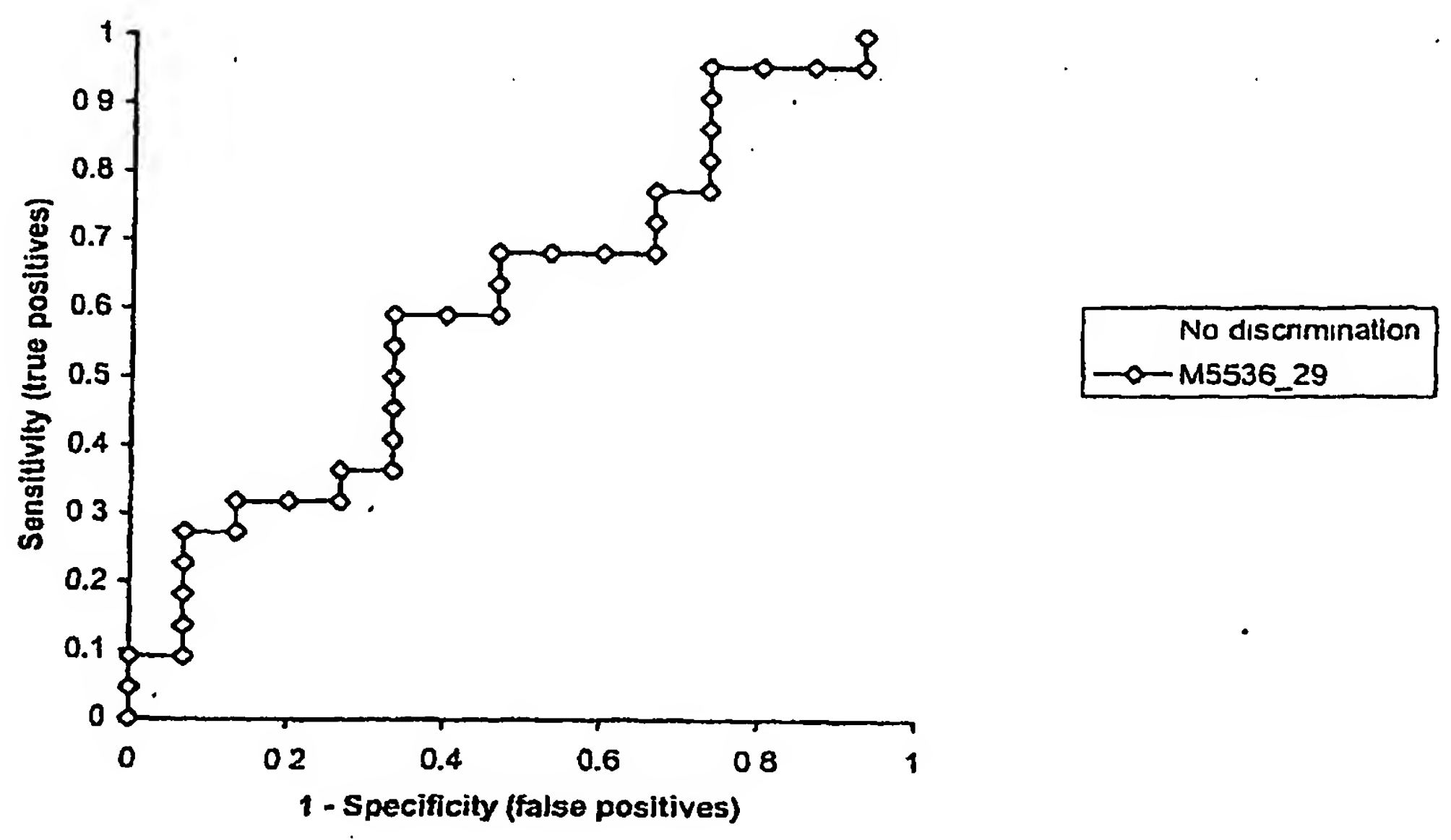
analysed with Analyse-it + Clinical Laboratory 16

| | | |
|--------------|---|------|
| Test | Receiver Operator Characteristic (ROC) curves | |
| | M5536_29 by SAMP_GRP | |
| Performed by | | Date |

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M5536_29 | 0.615 | 0.0950 | 0.1129 | 0.429 to 0.801 | have higher values |



| M5536_29
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 2.476873773 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

analysed with Analyse-it + Clinical Laboratory 16

Test Receiver Operator Characteristic (ROC) curves

M5536_29 by SAMP_GRP

| Performed by | | | | | | Date | |
|--------------|-------|--------|----|----|--|------|----|
| 2.735239337 | 95.5% | 6.7% | 21 | 1 | | 14 | 1 |
| 3.120351652 | 95.5% | 13.3% | 21 | 2 | | 13 | 1 |
| 3.38479814 | 95.5% | 20.0% | 21 | 3 | | 12 | 1 |
| 3.997539986 | 95.5% | 26.7% | 21 | 4 | | 11 | 1 |
| 4.095493334 | 90.9% | 26.7% | 20 | 4 | | 11 | 2 |
| 4.263146482 | 86.4% | 26.7% | 19 | 4 | | 11 | 3 |
| 4.594284377 | 81.8% | 26.7% | 18 | 4 | | 11 | 4 |
| 5.972410264 | 77.3% | 26.7% | 17 | 4 | | 11 | 5 |
| 6.664831963 | 77.3% | 33.3% | 17 | 5 | | 10 | 5 |
| 6.817705332 | 72.7% | 33.3% | 16 | 5 | | 10 | 6 |
| 8.141308021 | 68.2% | 33.3% | 15 | 5 | | 10 | 7 |
| 8.480803777 | 68.2% | 40.0% | 15 | 6 | | 9 | 7 |
| 8.987766361 | 68.2% | 46.7% | 15 | 7 | | 8 | 7 |
| 9.231911097 | 68.2% | 53.3% | 15 | 8 | | 7 | 7 |
| 9.552062697 | 63.6% | 53.3% | 14 | 8 | | 7 | 8 |
| 10.55353177 | 59.1% | 53.3% | 13 | 8 | | 7 | 9 |
| 13.97374817 | 59.1% | 60.0% | 13 | 9 | | 6 | 9 |
| 14.02278422 | 59.1% | 66.7% | 13 | 10 | | 5 | 9 |
| 14.88280435 | 54.5% | 66.7% | 12 | 10 | | 5 | 10 |
| 15.23628909 | 50.0% | 66.7% | 11 | 10 | | 5 | 11 |
| 23.4978088 | 45.5% | 66.7% | 10 | 10 | | 5 | 12 |
| 25.14900037 | 40.9% | 66.7% | 9 | 10 | | 5 | 13 |
| 26.02066777 | 36.4% | 66.7% | 8 | 10 | | 5 | 14 |
| 30.6345416 | 36.4% | 73.3% | 8 | 11 | | 4 | 14 |
| 30.77622328 | 31.8% | 73.3% | 7 | 11 | | 4 | 15 |
| 31.94867944 | 31.8% | 80.0% | 7 | 12 | | 3 | 15 |
| 34.49611418 | 31.8% | 86.7% | 7 | 13 | | 2 | 15 |
| 35.08171775 | 27.3% | 86.7% | 6 | 13 | | 2 | 16 |
| 36.99180982 | 27.3% | 93.3% | 6 | 14 | | 1 | 16 |
| 38.61874069 | 22.7% | 93.3% | 5 | 14 | | 1 | 17 |
| 41.37427345 | 18.2% | 93.3% | 4 | 14 | | 1 | 18 |
| 43.17627664 | 13.6% | 93.3% | 3 | 14 | | 1 | 19 |
| 44.48204224 | 9.1% | 93.3% | 2 | 14 | | 1 | 20 |
| 52.94519269 | 9.1% | 100.0% | 2 | 15 | | 0 | 20 |
| 62.35890391 | 4.5% | 100.0% | 1 | 15 | | 0 | 21 |
| 65.07263487 | 0.0% | 100.0% | 0 | 15 | | 0 | 22 |

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analysed with Analyse-It + Clinical Laboratory 1 62

Test Receiver Operator Characteristic (ROC) curves

M5632_34 by SAMP_GRP

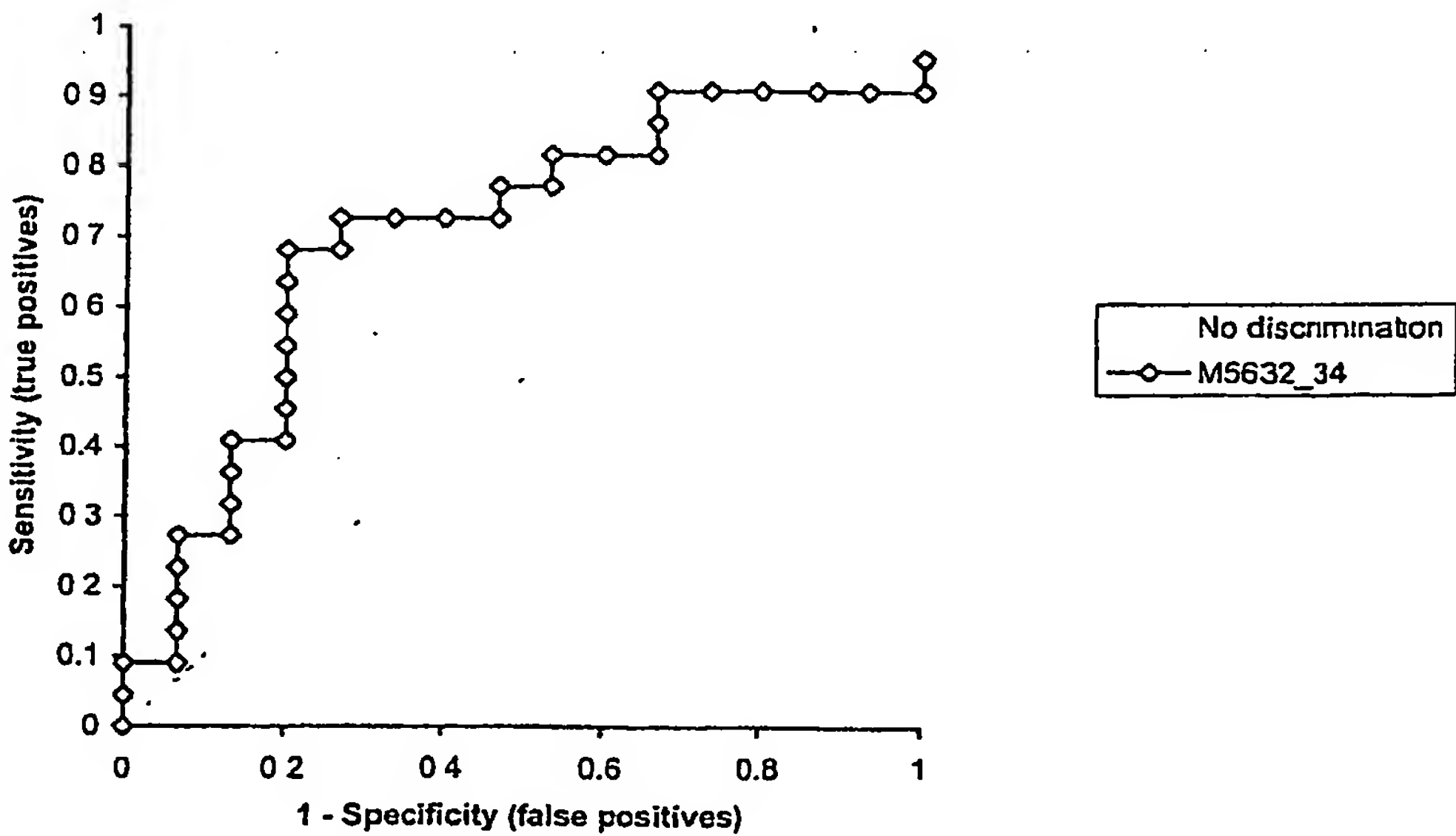
Performed by

Date

n 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M5632_34 | 0.706 | 0.0896 | 0.0107 | 0.530 to 0.882 | have higher values |



| M5632_34
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| -0.66241178 | 95.5% | 0.0% | 21 | 0 | 15 | 1 |

Test Receiver Operator Characteristic (ROC) curves

M5632_34 by SAMP_GRP

| Performed by | | | | | | Date | |
|--------------|-------|--------|----|----|----|------|--|
| -0.504040134 | 90.9% | 0.0% | 20 | 0 | 15 | 2 | |
| 0.388898772 | 90.9% | 6.7% | 20 | 1 | 14 | 2 | |
| 0.653349603 | 90.9% | 13.3% | 20 | 2 | 13 | 2 | |
| 0.77842974 | 90.9% | 20.0% | 20 | 3 | 12 | 2 | |
| 0.825697867 | 90.9% | 26.7% | 20 | 4 | 11 | 2 | |
| 0.968687382 | 90.9% | 33.3% | 20 | 5 | 10 | 2 | |
| 0.998569141 | 86.4% | 33.3% | 19 | 5 | 10 | 3 | |
| 1.077108899 | 81.8% | 33.3% | 18 | 5 | 10 | 4 | |
| 1.107048847 | 81.8% | 40.0% | 18 | 6 | 9 | 4 | |
| 1.126856905 | 81.8% | 46.7% | 18 | 7 | 8 | 4 | |
| 1.314607138 | 77.3% | 46.7% | 17 | 7 | 8 | 5 | |
| 1.596204729 | 77.3% | 53.3% | 17 | 8 | 7 | 5 | |
| 1.932708548 | 72.7% | 53.3% | 16 | 8 | 7 | 6 | |
| 1.975900376 | 72.7% | 60.0% | 16 | 9 | 6 | 6 | |
| 2.238214852 | 72.7% | 66.7% | 16 | 10 | 5 | 6 | |
| 2.251560917 | 72.7% | 73.3% | 16 | 11 | 4 | 6 | |
| 2.352154965 | 68.2% | 73.3% | 15 | 11 | 4 | 7 | |
| 2.521548392 | 68.2% | 80.0% | 15 | 12 | 3 | 7 | |
| 2.854528318 | 63.6% | 80.0% | 14 | 12 | 3 | 8 | |
| 3.024417527 | 59.1% | 80.0% | 13 | 12 | 3 | 9 | |
| 3.122910575 | 54.5% | 80.0% | 12 | 12 | 3 | 10 | |
| 3.488196703 | 50.0% | 80.0% | 11 | 12 | 3 | 11 | |
| 3.61290495 | 45.5% | 80.0% | 10 | 12 | 3 | 12 | |
| 3.841931455 | 40.9% | 80.0% | 9 | 12 | 3 | 13 | |
| 3.873274722 | 40.9% | 86.7% | 9 | 13 | 2 | 13 | |
| 4.550969293 | 36.4% | 86.7% | 8 | 13 | 2 | 14 | |
| 4.687454232 | 31.8% | 86.7% | 7 | 13 | 2 | 15 | |
| 5.820357958 | 27.3% | 86.7% | 6 | 13 | 2 | 16 | |
| 5.840106731 | 27.3% | 93.3% | 6 | 14 | 1 | 16 | |
| 6.139408278 | 22.7% | 93.3% | 5 | 14 | 1 | 17 | |
| 6.675787665 | 18.2% | 93.3% | 4 | 14 | 1 | 18 | |
| 10.06276664 | 13.6% | 93.3% | 3 | 14 | 1 | 19 | |
| 13.41667655 | 9.1% | 93.3% | 2 | 14 | 1 | 20 | |
| 14.98079515 | 9.1% | 100.0% | 2 | 15 | 0 | 20 | |
| 20.80876033 | 4.5% | 100.0% | 1 | 15 | 0 | 21 | |
| 28.92874487 | 0.0% | 100.0% | 0 | 15 | 0 | 22 | |

6.1 KD

analysed with Analyse-It + Clinical Laboratory 1 62

Test Receiver Operator Characteristic (ROC) curves

M6083_96 by SAMP_GRP

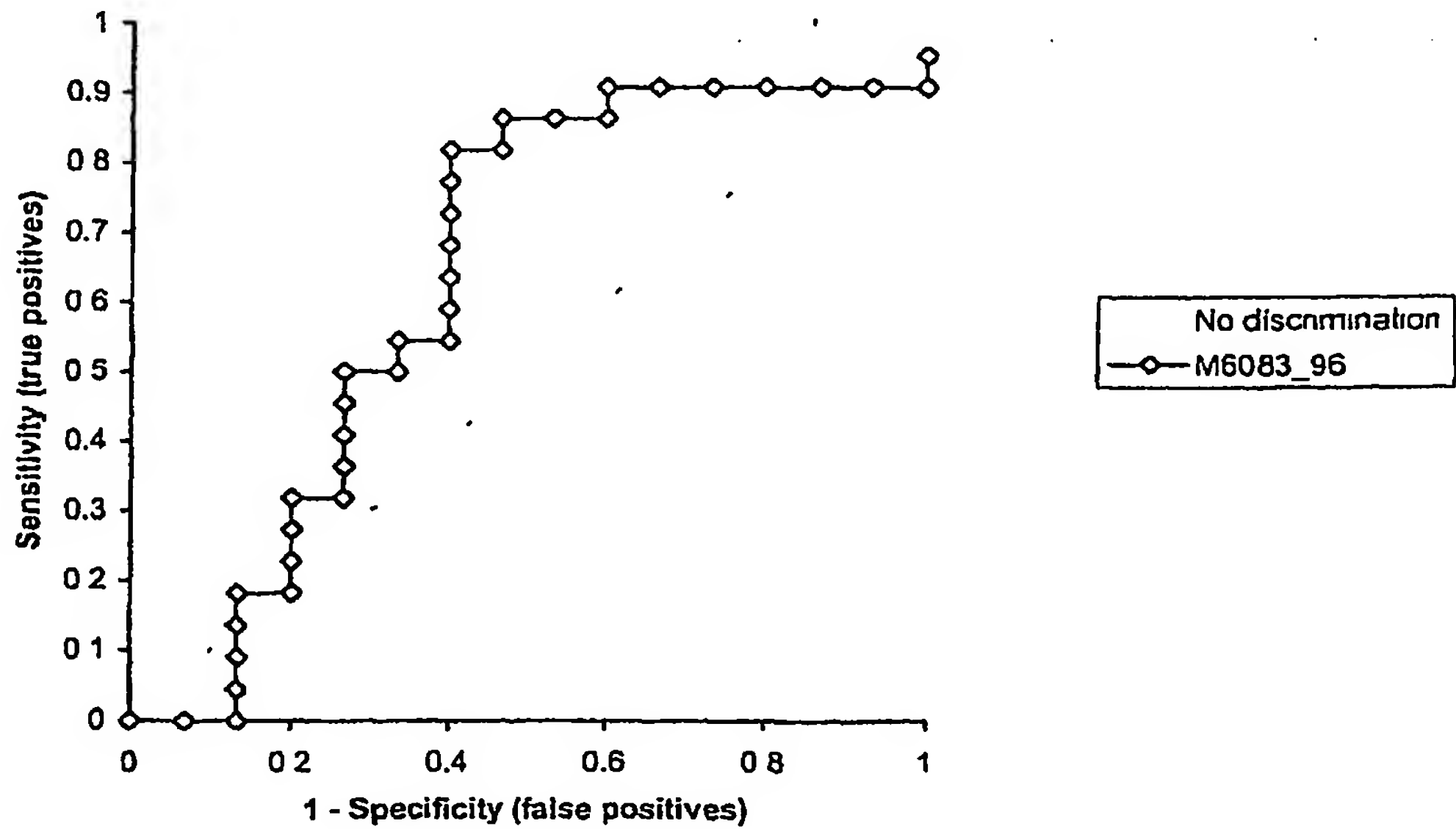
Performed by

Date

n 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M6083_96 | 0.636 | 0.1018 | 0.0903 | 0.437 to 0.836 | have higher values |



| M6083_96
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| -1.209303384 | 95.5% | 0.0% | 21 | 0 | 15 | 1 |

Test Receiver Operator Characteristic (ROC) curves

M6083_96 by SAMP_GRP

| Performed by | | | | | Date | |
|--------------|-------|--------|----|----|------|----|
| -0.840532557 | 90.9% | 0.0% | 20 | 0 | 15 | 2 |
| 0.051463134 | 90.9% | 6.7% | 20 | 1 | 14 | 2 |
| 0.706431918 | 90.9% | 13.3% | 20 | 2 | 13 | 2 |
| 1.124512015 | 90.9% | 20.0% | 20 | 3 | 12 | 2 |
| 1.591362646 | 90.9% | 26.7% | 20 | 4 | 11 | 2 |
| 1.683209049 | 90.9% | 33.3% | 20 | 5 | 10 | 2 |
| 1.788481249 | 90.9% | 40.0% | 20 | 6 | 9 | 2 |
| 2.481609046 | 86.4% | 40.0% | 19 | 6 | 9 | 3 |
| 2.51886446 | 86.4% | 46.7% | 19 | 7 | 8 | 3 |
| 2.55797428 | 86.4% | 53.3% | 19 | 8 | 7 | 3 |
| 2.605058174 | 81.8% | 53.3% | 18 | 8 | 7 | 4 |
| 2.885215545 | 81.8% | 60.0% | 18 | 9 | 6 | 4 |
| 3.197459448 | 77.3% | 60.0% | 17 | 9 | 6 | 5 |
| 3.365272297 | 72.7% | 60.0% | 16 | 9 | 6 | 6 |
| 3.671798165 | 68.2% | 60.0% | 15 | 9 | 6 | 7 |
| 3.90007016 | 63.6% | 60.0% | 14 | 9 | 6 | 8 |
| 4.039270694 | 59.1% | 60.0% | 13 | 9 | 6 | 9 |
| 4.436064311 | 54.5% | 60.0% | 12 | 9 | 6 | 10 |
| 4.617136392 | 54.5% | 66.7% | 12 | 10 | 5 | 10 |
| 5.115352999 | 50.0% | 66.7% | 11 | 10 | 5 | 11 |
| 6.353216703 | 50.0% | 73.3% | 11 | 11 | 4 | 11 |
| 6.4912197 | 45.5% | 73.3% | 10 | 11 | 4 | 12 |
| 7.441252266 | 40.9% | 73.3% | 9 | 11 | 4 | 13 |
| 8.792126385 | 36.4% | 73.3% | 8 | 11 | 4 | 14 |
| 11.29691249 | 31.8% | 73.3% | 7 | 11 | 4 | 15 |
| 13.30488137 | 31.8% | 80.0% | 7 | 12 | 3 | 15 |
| 13.92938769 | 27.3% | 80.0% | 6 | 12 | 3 | 16 |
| 15.8894186 | 22.7% | 80.0% | 5 | 12 | 3 | 17 |
| 15.99529578 | 18.2% | 80.0% | 4 | 12 | 3 | 18 |
| 17.73356817 | 18.2% | 86.7% | 4 | 13 | 2 | 18 |
| 20.46026717 | 13.6% | 86.7% | 3 | 13 | 2 | 19 |
| 21.31066896 | 9.1% | 86.7% | 2 | 13 | 2 | 20 |
| 23.17512833 | 4.5% | 86.7% | 1 | 13 | 2 | 21 |
| 29.15341734 | 0.0% | 86.7% | 0 | 13 | 2 | 22 |
| 37.84621415 | 0.0% | 93.3% | 0 | 14 | 1 | 22 |
| 43.82802395 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

6.4/20

Test Receiver Operator Characteristic (ROC) curves

M6406_04 by SAMP_GRP

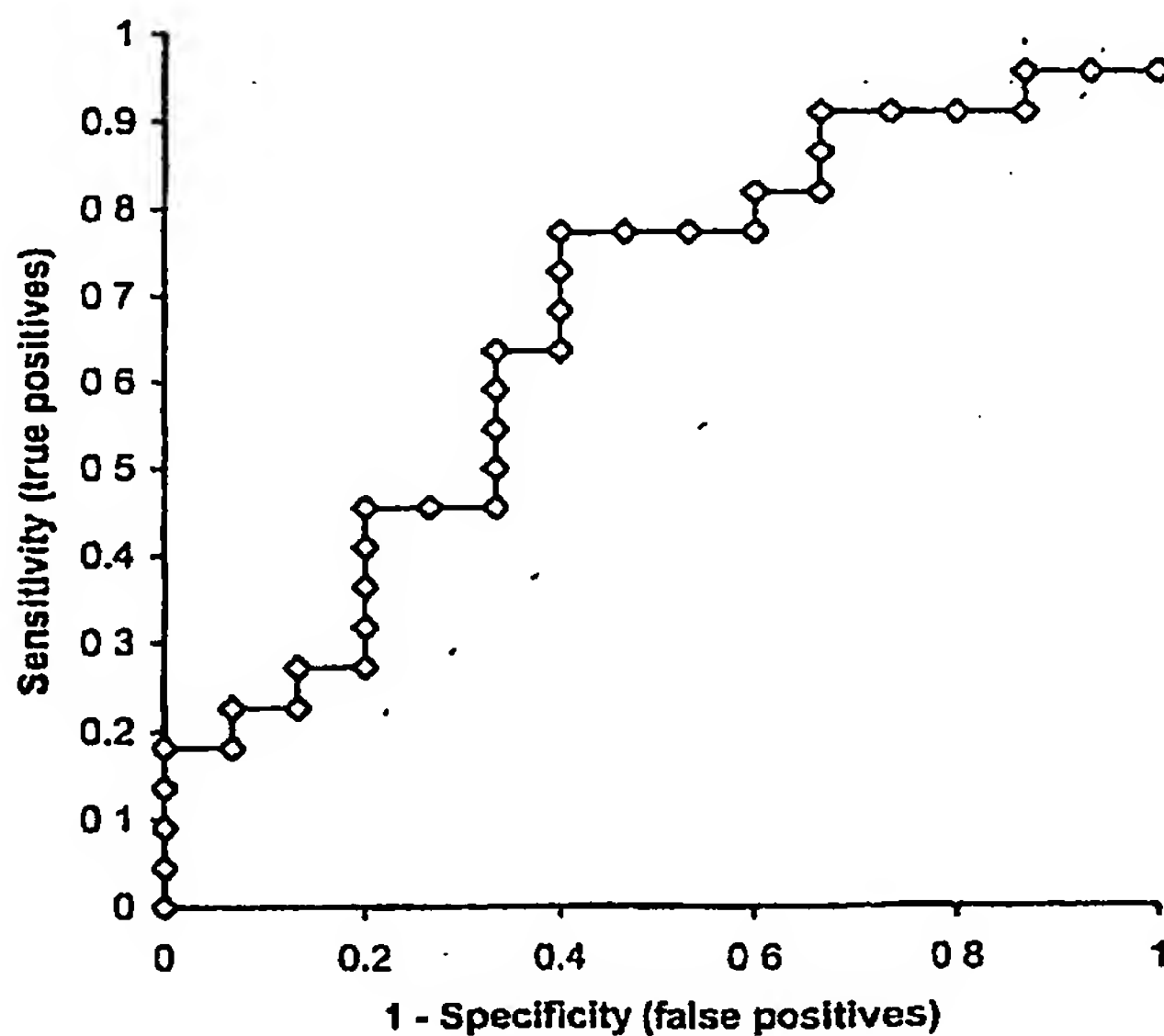
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M6406_04 | 0.667 | 0.0918 | 0.0348 | 0.487 to 0.847 | have higher values |



| M6406_04
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 0.207686614 | 95.5% | 0.0% | 21 | 0 | 15 | 1 |

Test Receiver Operator Characteristic (ROC) curves

M6406_04 by SAMP_GRP

| Performed by | | | | | Date | |
|--------------|-------|--------|----|----|------|----|
| 0.923420696 | 95.5% | 6.7% | 21 | 1 | 14 | 1 |
| 1.234313198 | 95.5% | 13.3% | 21 | 2 | 13 | 1 |
| 1.494874412 | 90.9% | 13.3% | 20 | 2 | 13 | 2 |
| 1.625003803 | 90.9% | 20.0% | 20 | 3 | 12 | 2 |
| 1.783038312 | 90.9% | 26.7% | 20 | 4 | 11 | 2 |
| 2.266399527 | 90.9% | 33.3% | 20 | 5 | 10 | 2 |
| 2.694941007 | 86.4% | 33.3% | 19 | 5 | 10 | 3 |
| 2.886712812 | 81.8% | 33.3% | 18 | 5 | 10 | 4 |
| 3.057125428 | 81.8% | 40.0% | 18 | 6 | 9 | 4 |
| 3.078671506 | 77.3% | 40.0% | 17 | 6 | 9 | 5 |
| 3.136138812 | 77.3% | 46.7% | 17 | 7 | 8 | 5 |
| 3.37282052 | 77.3% | 53.3% | 17 | 8 | 7 | 5 |
| 3.386309735 | 77.3% | 60.0% | 17 | 9 | 6 | 5 |
| 3.470325094 | 72.7% | 60.0% | 16 | 9 | 6 | 6 |
| 3.510408777 | 68.2% | 60.0% | 15 | 9 | 6 | 7 |
| 3.702964632 | 63.6% | 60.0% | 14 | 9 | 6 | 8 |
| 4.134558043 | 63.6% | 66.7% | 14 | 10 | 5 | 8 |
| 4.418528395 | 59.1% | 66.7% | 13 | 10 | 5 | 9 |
| 4.626183014 | 54.5% | 66.7% | 12 | 10 | 5 | 10 |
| 6.199219603 | 50.0% | 66.7% | 11 | 10 | 5 | 11 |
| 6.643154701 | 45.5% | 66.7% | 10 | 10 | 5 | 12 |
| 6.801405828 | 45.5% | 73.3% | 10 | 11 | 4 | 12 |
| 8.678907807 | 45.5% | 80.0% | 10 | 12 | 3 | 12 |
| 8.928059882 | 40.9% | 80.0% | 9 | 12 | 3 | 13 |
| 9.547872707 | 36.4% | 80.0% | 8 | 12 | 3 | 14 |
| 9.740209204 | 31.8% | 80.0% | 7 | 12 | 3 | 15 |
| 11.50928318 | 27.3% | 80.0% | 6 | 12 | 3 | 16 |
| 11.64666186 | 27.3% | 86.7% | 6 | 13 | 2 | 16 |
| 16.68248737 | 22.7% | 86.7% | 5 | 13 | 2 | 17 |
| 18.36670762 | 22.7% | 93.3% | 5 | 14 | 1 | 17 |
| 20.99571285 | 18.2% | 93.3% | 4 | 14 | 1 | 18 |
| 26.53742371 | 18.2% | 100.0% | 4 | 15 | 0 | 18 |
| 28.29947448 | 13.6% | 100.0% | 3 | 15 | 0 | 19 |
| 48.99553133 | 9.1% | 100.0% | 2 | 15 | 0 | 20 |
| 75.56336781 | 4.5% | 100.0% | 1 | 15 | 0 | 21 |
| 727.9817302 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

6.5 KD

Test Receiver Operator Characteristic (ROC) curves

M6468_89 by SAMP_GRP

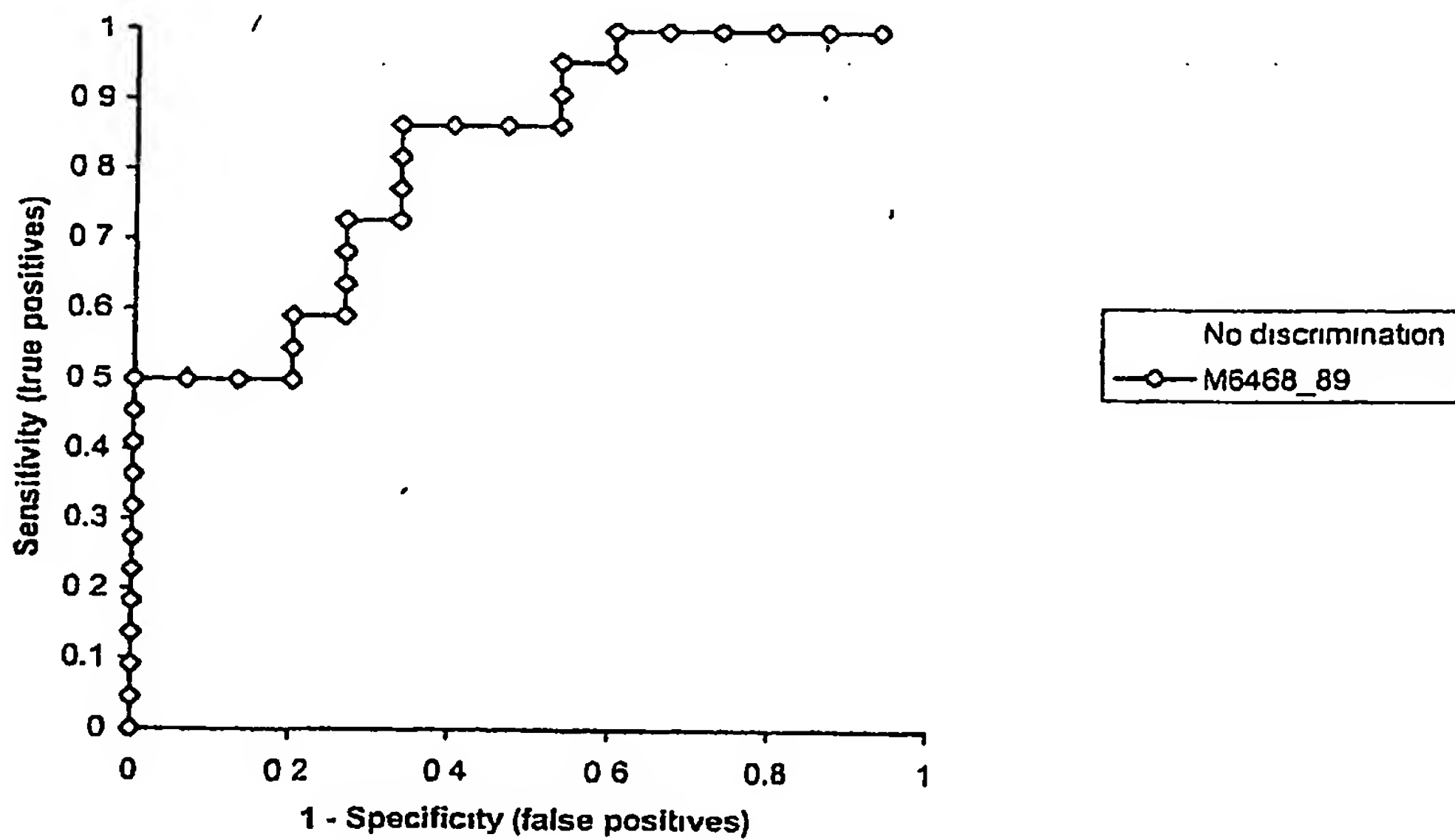
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|---------|----------------|--------------------|
| M6468_89 | 0.824 | 0.0679 | <0.0001 | 0.691 to 0.957 | have higher values |



| M6468_89
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 0.091826597 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

Test Receiver Operator Characteristic (ROC) curves

M6468_89 by SAMP_GRP

| Performed by | | | | | Date | | | |
|--------------|--------|--------|----|----|------|----|--|--|
| 0.835563258 | 100.0% | 13.3% | 22 | 2 | 13 | 0 | | |
| 0.93219296 | 100 0% | 20.0% | 22 | 3 | 12 | 0 | | |
| 1.074969489 | 100.0% | 26.7% | 22 | 4 | 11 | 0 | | |
| 1.133243299 | 100 0% | 33.3% | 22 | 5 | 10 | 0 | | |
| 1.518080502 | 100.0% | 40.0% | 22 | 6 | 9 | 0 | | |
| 1.825078341 | 95.5% | 40.0% | 21 | 6 | 9 | 1 | | |
| 1.918368848 | 95.5% | 46.7% | 21 | 7 | 8 | 1 | | |
| 2.230152821 | 90.9% | 46.7% | 20 | 7 | 8 | 2 | | |
| 2.375750164 | 86.4% | 46.7% | 19 | 7 | 8 | 3 | | |
| 2.641109179 | 86.4% | 53.3% | 19 | 8 | 7 | 3 | | |
| 3.094798916 | 86.4% | 60.0% | 19 | 9 | 6 | 3 | | |
| 3.811488644 | 86.4% | 66.7% | 19 | 10 | 5 | 3 | | |
| 4.500641184 | 81 8% | 66 7% | 18 | 10 | 5 | 4 | | |
| 4.783912451 | 77.3% | 66.7% | 17 | 10 | 5 | 5 | | |
| 4.794961294 | 72.7% | 66.7% | 16 | 10 | 5 | 6 | | |
| 4.934982572 | 72.7% | 73.3% | 16 | 11 | 4 | 6 | | |
| 5.034285335 | 68.2% | 73 3% | 15 | 11 | 4 | 7 | | |
| 5.077822723 | 63 6% | 73 3% | 14 | 11 | 4 | 8 | | |
| 5.983764713 | 59.1% | 73.3% | 13 | 11 | 4 | 9 | | |
| 7.45907997 | 59.1% | 80.0% | 13 | 12 | 3 | 9 | | |
| 7.491795742 | 54 5% | 80 0% | 12 | 12 | 3 | 10 | | |
| 8.139771712 | 50 0% | 80 0% | 11 | 12 | 3 | 11 | | |
| 8.555474896 | 50.0% | 86 7% | 11 | 13 | 2 | 11 | | |
| 9.467190147 | 50.0% | 93.3% | 11 | 14 | 1 | 11 | | |
| 9.887556218 | 50 0% | 100 0% | 11 | 15 | 0 | 11 | | |
| 12.78727407 | 45.5% | 100 0% | 10 | 15 | 0 | 12 | | |
| 14.99572961 | 40 9% | 100.0% | 9 | 15 | 0 | 13 | | |
| 15.17972908 | 36 4% | 100 0% | 8 | 15 | 0 | 14 | | |
| 16.21889052 | 31 8% | 100 0% | 7 | 15 | 0 | 15 | | |
| 16.78423313 | 27 3% | 100.0% | 6 | 15 | 0 | 16 | | |
| 17.96332953 | 22.7% | 100.0% | 5 | 15 | 0 | 17 | | |
| 26.72227163 | 18.2% | 100.0% | 4 | 15 | 0 | 18 | | |
| 31.20758175 | 13.6% | 100.0% | 3 | 15 | 0 | 19 | | |
| 57.91100778 | 9.1% | 100.0% | 2 | 15 | 0 | 20 | | |
| 107.7567031 | 4 5% | 100.0% | 1 | 15 | 0 | 21 | | |
| 426.7508851 | 0.0% | 100.0% | 0 | 15 | 0 | 22 | | |

M6602_76 by SAMP_GRP

Date

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

The figure is a Receiver Operating Characteristic (ROC) curve. The y-axis is labeled 'Sensitivity (true positives)' and ranges from 0 to 1. The x-axis is labeled '1 - Specificity (false positives)' and ranges from 0 to 1. The curve for 'M6602_76' starts at (0,0) and follows a step-like path, reaching a sensitivity of approximately 0.95 at a 1-specificity of 0.8. A legend in the bottom right corner shows a horizontal line with a diamond marker for 'M6602_76' and the text 'No discrimination' above it.

| 1 - Specificity (false positives) | Sensitivity (true positives) |
|-----------------------------------|------------------------------|
| 0.00 | 0.00 |
| 0.01 | 0.05 |
| 0.02 | 0.10 |
| 0.03 | 0.15 |
| 0.04 | 0.20 |
| 0.05 | 0.25 |
| 0.06 | 0.30 |
| 0.07 | 0.32 |
| 0.08 | 0.32 |
| 0.09 | 0.32 |
| 0.10 | 0.32 |
| 0.11 | 0.32 |
| 0.12 | 0.32 |
| 0.13 | 0.32 |
| 0.14 | 0.32 |
| 0.15 | 0.32 |
| 0.16 | 0.32 |
| 0.17 | 0.32 |
| 0.18 | 0.32 |
| 0.19 | 0.32 |
| 0.20 | 0.32 |
| 0.21 | 0.32 |
| 0.22 | 0.32 |
| 0.23 | 0.32 |
| 0.24 | 0.32 |
| 0.25 | 0.32 |
| 0.26 | 0.32 |
| 0.27 | 0.32 |
| 0.28 | 0.32 |
| 0.29 | 0.32 |
| 0.30 | 0.32 |
| 0.31 | 0.32 |
| 0.32 | 0.32 |
| 0.33 | 0.32 |
| 0.34 | 0.32 |
| 0.35 | 0.32 |
| 0.36 | 0.32 |
| 0.37 | 0.32 |
| 0.38 | 0.32 |
| 0.39 | 0.32 |
| 0.40 | 0.32 |
| 0.41 | 0.32 |
| 0.42 | 0.32 |
| 0.43 | 0.32 |
| 0.44 | 0.32 |
| 0.45 | 0.32 |
| 0.46 | 0.32 |
| 0.47 | 0.32 |
| 0.48 | 0.32 |
| 0.49 | 0.32 |
| 0.50 | 0.32 |
| 0.51 | 0.32 |
| 0.52 | 0.32 |
| 0.53 | 0.32 |
| 0.54 | 0.32 |
| 0.55 | 0.32 |
| 0.56 | 0.32 |
| 0.57 | 0.32 |
| 0.58 | 0.32 |
| 0.59 | 0.32 |
| 0.60 | 0.32 |
| 0.61 | 0.32 |
| 0.62 | 0.32 |
| 0.63 | 0.32 |
| 0.64 | 0.32 |
| 0.65 | 0.32 |
| 0.66 | 0.32 |
| 0.67 | 0.32 |
| 0.68 | 0.32 |
| 0.69 | 0.32 |
| 0.70 | 0.32 |
| 0.71 | 0.32 |
| 0.72 | 0.32 |
| 0.73 | 0.32 |
| 0.74 | 0.32 |
| 0.75 | 0.32 |
| 0.76 | 0.32 |
| 0.77 | 0.32 |
| 0.78 | 0.32 |
| 0.79 | 0.32 |
| 0.80 | 0.32 |
| 0.81 | 0.32 |
| 0.82 | 0.32 |
| 0.83 | 0.32 |
| 0.84 | 0.32 |
| 0.85 | 0.32 |
| 0.86 | 0.32 |
| 0.87 | 0.32 |
| 0.88 | 0.32 |
| 0.89 | 0.32 |
| 0.90 | 0.32 |
| 0.91 | 0.32 |
| 0.92 | 0.32 |
| 0.93 | 0.32 |
| 0.94 | 0.32 |
| 0.95 | 0.32 |
| 0.96 | 0.32 |
| 0.97 | 0.32 |
| 0.98 | 0.32 |
| 0.99 | 0.32 |
| 1.00 | 0.32 |

66

Test Receiver Operator Characteristic (ROC) curves

M6602_76 by SAMP_GRP

| Performed by | | | | | Date | |
|--------------|-------|--------|----|----|------|----|
| 1.145943829 | 95.5% | 6.7% | 21 | 1 | 14 | 1 |
| 1.271587635 | 95.5% | 13.3% | 21 | 2 | 13 | 1 |
| 1.319340027 | 95.5% | 20.0% | 21 | 3 | 12 | 1 |
| 1.413613659 | 90.9% | 20.0% | 20 | 3 | 12 | 2 |
| 1.430941938 | 90.9% | 26.7% | 20 | 4 | 11 | 2 |
| 1.499030655 | 90.9% | 33.3% | 20 | 5 | 10 | 2 |
| 2.982147717 | 90.9% | 40.0% | 20 | 6 | 9 | 2 |
| 3.310303594 | 90.9% | 46.7% | 20 | 7 | 8 | 2 |
| 3.583311101 | 90.9% | 53.3% | 20 | 8 | 7 | 2 |
| 3.910654764 | 90.9% | 60.0% | 20 | 9 | 6 | 2 |
| 4.106539181 | 86.4% | 60.0% | 19 | 9 | 6 | 3 |
| 4.146892007 | 81.8% | 60.0% | 18 | 9 | 6 | 4 |
| 4.504318001 | 77.3% | 60.0% | 17 | 9 | 6 | 5 |
| 5.125117622 | 77.3% | 66.7% | 17 | 10 | 5 | 5 |
| 6.118715467 | 77.3% | 73.3% | 17 | 11 | 4 | 5 |
| 6.530734839 | 72.7% | 73.3% | 16 | 11 | 4 | 6 |
| 8.485693053 | 68.2% | 73.3% | 15 | 11 | 4 | 7 |
| 8.701819799 | 63.6% | 73.3% | 14 | 11 | 4 | 8 |
| 8.938297048 | 63.6% | 80.0% | 14 | 12 | 3 | 8 |
| 11.54358186 | 59.1% | 80.0% | 13 | 12 | 3 | 9 |
| 11.77637501 | 54.5% | 80.0% | 12 | 12 | 3 | 10 |
| 13.17815594 | 50.0% | 80.0% | 11 | 12 | 3 | 11 |
| 14.70426566 | 45.5% | 80.0% | 10 | 12 | 3 | 12 |
| 18.11626496 | 40.9% | 80.0% | 9 | 12 | 3 | 13 |
| 20.74477865 | 40.9% | 86.7% | 9 | 13 | 2 | 13 |
| 21.72001082 | 40.9% | 93.3% | 9 | 14 | 1 | 13 |
| 22.61295945 | 36.4% | 93.3% | 8 | 14 | 1 | 14 |
| 28.44256416 | 31.8% | 93.3% | 7 | 14 | 1 | 15 |
| 28.59767222 | 31.8% | 100.0% | 7 | 15 | 0 | 15 |
| 31.1639502 | 27.3% | 100.0% | 6 | 15 | 0 | 16 |
| 34.82375034 | 22.7% | 100.0% | 5 | 15 | 0 | 17 |
| 36.530145 | 18.2% | 100.0% | 4 | 15 | 0 | 18 |
| 68.51218679 | 13.6% | 100.0% | 3 | 15 | 0 | 19 |
| 72.06446204 | 9.1% | 100.0% | 2 | 15 | 0 | 20 |
| 76.93895384 | 4.5% | 100.0% | 1 | 15 | 0 | 21 |
| 1132.766318 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

Test Receiver Operator Characteristic (ROC) curves

M6678_13 by SAMP_GRP

| Performed by | | | | | | Date | |
|--------------|--------|--------|----|----|----|------|--|
| 0.804078156 | 100.0% | 13.3% | 22 | 2 | 13 | 0 | |
| 0.947881336 | 100.0% | 20.0% | 22 | 3 | 12 | 0 | |
| 1.776830937 | 100 0% | 26.7% | 22 | 4 | 11 | 0 | |
| 1.815583274 | 100 0% | 33.3% | 22 | 5 | 10 | 0 | |
| 1.87952221 | 100.0% | 40.0% | 22 | 6 | 9 | 0 | |
| 2.215304578 | 95.5% | 40 0% | 21 | 6 | 9 | 1 | |
| 2.686887113 | 90 9% | 40 0% | 20 | 6 | 9 | 2 | |
| 3.418198784 | 90.9% | 46.7% | 20 | 7 | 8 | 2 | |
| 3.569813842 | 90.9% | 53 3% | 20 | 8 | 7 | 2 | |
| 4.140555716 | 90.9% | 60.0% | 20 | 9 | 6 | 2 | |
| 4.854915071 | 86 4% | 60.0% | 19 | 9 | 6 | 3 | |
| 4.910729785 | 81.8% | 60.0% | 18 | 9 | 6 | 4 | |
| 7.495729351 | 77 3% | 60 0% | 17 | 9 | 6 | 5 | |
| 7.529526451 | 77.3% | 66.7% | 17 | 10 | 5 | 5 | |
| 8.141631464 | 72 7% | 66.7% | 16 | 10 | 5 | 6 | |
| 8.894175505 | 68.2% | 66.7% | 15 | 10 | 5 | 7 | |
| 9.897687452 | 68.2% | 73 3% | 15 | 11 | 4 | 7 | |
| 10.70496756 | 63 6% | 73 3% | 14 | 11 | 4 | 8 | |
| 11.04636753 | 63.6% | 80 0% | 14 | 12 | 3 | 8 | |
| 11.87418655 | 59.1% | 80 0% | 13 | 12 | 3 | 9 | |
| 12.11700223 | 59.1% | 86.7% | 13 | 13 | 2 | 9 | |
| 12.99470979 | 54.5% | 86.7% | 12 | 13 | 2 | 10 | |
| 15.29949571 | 50.0% | 86.7% | 11 | 13 | 2 | 11 | |
| 15.49869338 | 45.5% | 86.7% | 10 | 13 | 2 | 12 | |
| 17.01670817 | 45 5% | 93 3% | 10 | 14 | 1 | 12 | |
| 17.39670531 | 45.5% | 100.0% | 10 | 15 | 0 | 12 | |
| 21.15304525 | 40.9% | 100 0% | 9 | 15 | 0 | 13 | |
| 25.24524975 | 36.4% | 100.0% | 8 | 15 | 0 | 14 | |
| 26.35790954 | 31 8% | 100.0% | 7 | 15 | 0 | 15 | |
| 40.71351756 | 27.3% | 100.0% | 6 | 15 | 0 | 16 | |
| 49.3578222 | 22.7% | 100.0% | 5 | 15 | 0 | 17 | |
| 54.7182916 | 18 2% | 100.0% | 4 | 15 | 0 | 18 | |
| 62.09784715 | 13.6% | 100.0% | 3 | 15 | 0 | 19 | |
| 66.98593778 | 9 1% | 100.0% | 2 | 15 | 0 | 20 | |
| 112.5819998 | 4.5% | 100.0% | 1 | 15 | 0 | 21 | |
| 421.1384813 | 0.0% | 100 0% | 0 | 15 | 0 | 22 | |

6.8 KP

Test | Receiver Operator Characteristic (ROC) curves

M6812_97 by SAMP_GRP

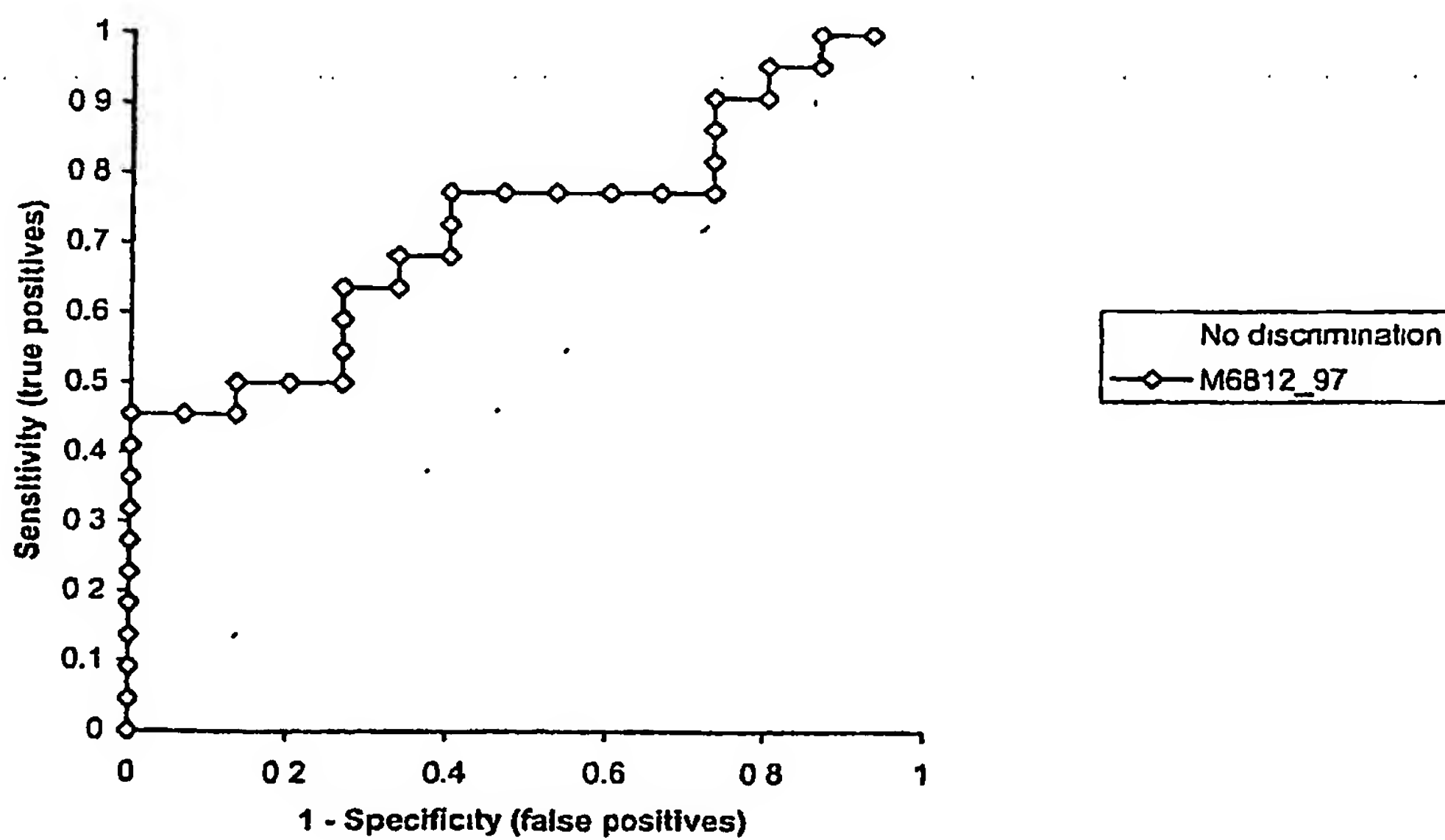
Performed by

Date _____

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M6812_97 | 0.730 | 0.0820 | 0.0025 | 0.570 to 0.891 | have higher values |



| M6812_97
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 0.00087157 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

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analysed with Analyse-It + Clinical Laboratory 1.6

| Test | | Receiver Operator Characteristic (ROC) curves | | | | | |
|--------------|--------|---|----|----|----|----|--|
| | | M6812_97 by SAMP_GRP | | | | | |
| Performed by | | Date | | | | | |
| 0.083697961 | 100.0% | 13.3% | 22 | 2 | 13 | 0 | |
| 0.10179494 | 95.5% | 13.3% | 21 | 2 | 13 | 1 | |
| 0.525080407 | 95.5% | 20.0% | 21 | 3 | 12 | 1 | |
| 0.570354396 | 90.9% | 20.0% | 20 | 3 | 12 | 2 | |
| 0.753188459 | 90.9% | 26.7% | 20 | 4 | 11 | 2 | |
| 1.11285706 | 86.4% | 26.7% | 19 | 4 | 11 | 3 | |
| 1.325208389 | 81.8% | 26.7% | 18 | 4 | 11 | 4 | |
| 1.617507376 | 77.3% | 26.7% | 17 | 4 | 11 | 5 | |
| 1.80310697 | 77.3% | 33.3% | 17 | 5 | 10 | 5 | |
| 1.839397793 | 77.3% | 40.0% | 17 | 6 | 9 | 5 | |
| 1.883035656 | 77.3% | 46.7% | 17 | 7 | 8 | 5 | |
| 2.134774398 | 77.3% | 53.3% | 17 | 8 | 7 | 5 | |
| 2.549415178 | 77.3% | 60.0% | 17 | 9 | 6 | 5 | |
| 2.737012635 | 72.7% | 60.0% | 16 | 9 | 6 | 6 | |
| 3.440345493 | 68.2% | 60.0% | 15 | 9 | 6 | 7 | |
| 3.760823507 | 68.2% | 66.7% | 15 | 10 | 5 | 7 | |
| 4.001239542 | 63.6% | 66.7% | 14 | 10 | 5 | 8 | |
| 4.235485182 | 63.6% | 73.3% | 14 | 11 | 4 | 8 | |
| 4.984817763 | 59.1% | 73.3% | 13 | 11 | 4 | 9 | |
| 5.108312165 | 54.5% | 73.3% | 12 | 11 | 4 | 10 | |
| 5.445686923 | 50.0% | 73.3% | 11 | 11 | 4 | 11 | |
| 6.569652629 | 50.0% | 80.0% | 11 | 12 | 3 | 11 | |
| 8.295531625 | 50.0% | 86.7% | 11 | 13 | 2 | 11 | |
| 10.26293153 | 45.5% | 86.7% | 10 | 13 | 2 | 12 | |
| 10.41860259 | 45.5% | 93.3% | 10 | 14 | 1 | 12 | |
| 10.54561463 | 45.5% | 100.0% | 10 | 15 | 0 | 12 | |
| 10.93678783 | 40.9% | 100.0% | 9 | 15 | 0 | 13 | |
| 13.079319 | 36.4% | 100.0% | 8 | 15 | 0 | 14 | |
| 14.73918594 | 31.8% | 100.0% | 7 | 15 | 0 | 15 | |
| 15.85800335 | 27.3% | 100.0% | 6 | 15 | 0 | 16 | |
| 17.43916435 | 22.7% | 100.0% | 5 | 15 | 0 | 17 | |
| 21.54469853 | 18.2% | 100.0% | 4 | 15 | 0 | 18 | |
| 26.33373752 | 13.6% | 100.0% | 3 | 15 | 0 | 19 | |
| 34.98959324 | 9.1% | 100.0% | 2 | 15 | 0 | 20 | |
| 78.8916841 | 4.5% | 100.0% | 1 | 15 | 0 | 21 | |
| 349.5455888 | 0.0% | 100.0% | 0 | 15 | 0 | 22 | |

7.0 KD

Test Receiver Operator Characteristic (ROC) curves

analysed with Analyse-it + Clinical Laboratory

M6995_07 by SAMP_GRP

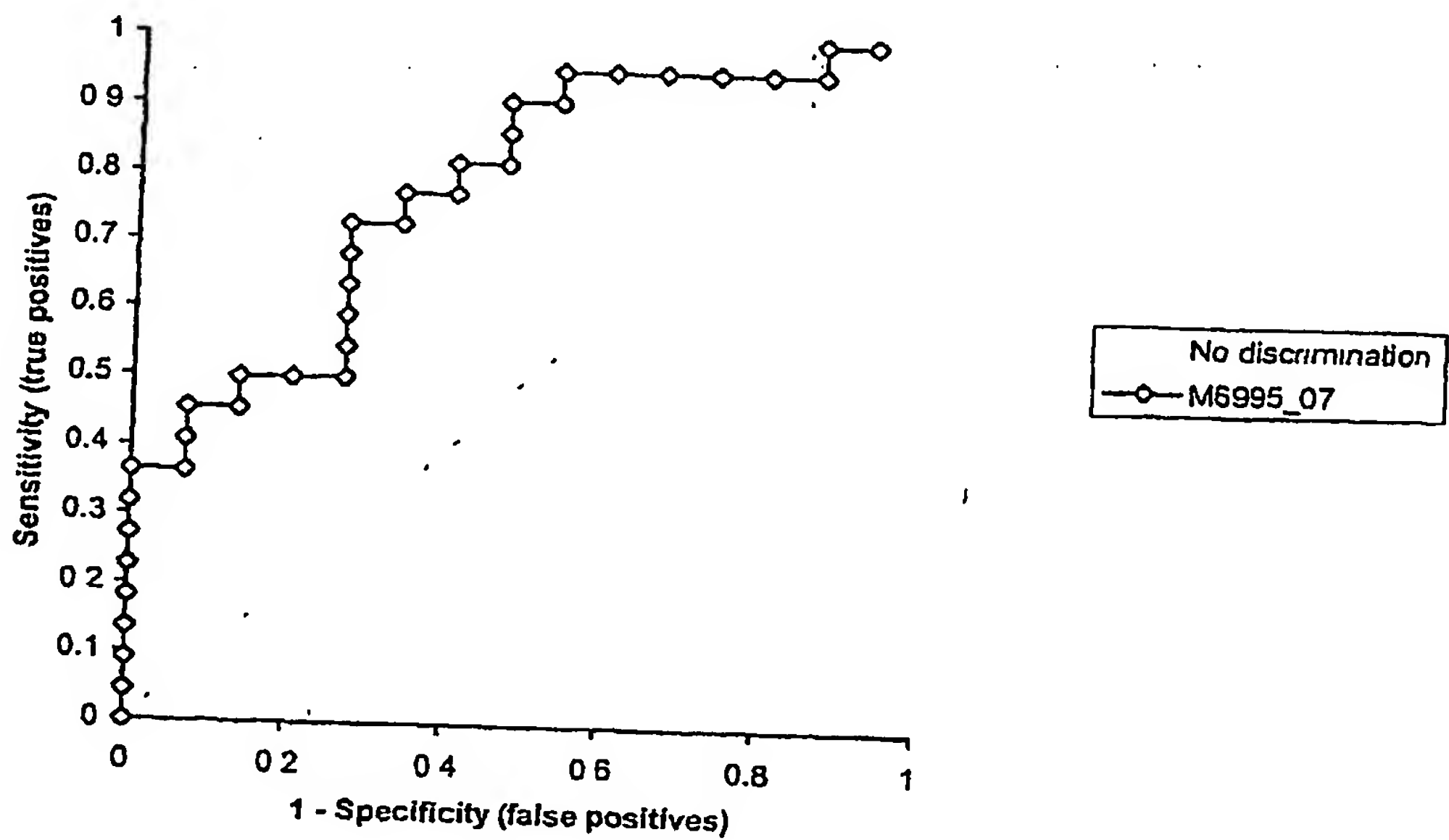
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|---------|----------------|--------------------|
| M6995_07 | 0.788 | 0.0754 | <0.0001 | 0.640 to 0.936 | have higher values |



| M6995_07
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 1.491443956 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

Test Receiver Operator Characteristic (ROC) curves

M6995_07 by SAMP_GRP

| Performed by | Date | | | | | |
|--------------|--------|--------|----|----|----|----|
| 3.064382087 | 100.0% | 13.3% | 22 | 2 | 13 | 0 |
| 3.211056923 | 95.5% | 13.3% | 21 | 2 | 13 | 1 |
| 3.575587562 | 95.5% | 20.0% | 21 | 3 | 12 | 1 |
| 3.590078119 | 95.5% | 26.7% | 21 | 4 | 11 | 1 |
| 3.64230464 | 95.5% | 33.3% | 21 | 5 | 10 | 1 |
| 3.810235534 | 95.5% | 40.0% | 21 | 6 | 9 | 1 |
| 6.561735067 | 95.5% | 46.7% | 21 | 7 | 8 | 1 |
| 6.569795399 | 90.9% | 46.7% | 20 | 7 | 8 | 2 |
| 6.985274137 | 90.9% | 53.3% | 20 | 8 | 7 | 2 |
| 7.844524644 | 86.4% | 53.3% | 19 | 8 | 7 | 3 |
| 8.233274241 | 81.8% | 53.3% | 18 | 8 | 7 | 4 |
| 8.552871855 | 81.8% | 60.0% | 18 | 9 | 6 | 4 |
| 8.581003414 | 77.3% | 60.0% | 17 | 9 | 6 | 5 |
| 9.276961217 | 77.3% | 66.7% | 17 | 10 | 5 | 5 |
| 9.71746827 | 72.7% | 66.7% | 16 | 10 | 5 | 6 |
| 10.65779175 | 72.7% | 73.3% | 16 | 11 | 4 | 6 |
| 12.8063091 | 68.2% | 73.3% | 15 | 11 | 4 | 7 |
| 14.37145601 | 63.6% | 73.3% | 14 | 11 | 4 | 8 |
| 14.46510595 | 59.1% | 73.3% | 13 | 11 | 4 | 9 |
| 14.51627012 | 54.5% | 73.3% | 12 | 11 | 4 | 10 |
| 14.94070151 | 50.0% | 73.3% | 11 | 11 | 4 | 11 |
| 17.48944524 | 50.0% | 80.0% | 11 | 12 | 3 | 11 |
| 20.38931912 | 50.0% | 86.7% | 11 | 13 | 2 | 11 |
| 20.4113395 | 45.5% | 86.7% | 10 | 13 | 2 | 12 |
| 25.92763801 | 45.5% | 93.3% | 10 | 14 | 1 | 12 |
| 26.40659722 | 40.9% | 93.3% | 9 | 14 | 1 | 13 |
| 26.74725392 | 36.4% | 93.3% | 8 | 14 | 1 | 14 |
| 32.42243868 | 36.4% | 100.0% | 8 | 15 | 0 | 14 |
| 38.44615454 | 31.8% | 100.0% | 7 | 15 | 0 | 15 |
| 39.5757897 | 27.3% | 100.0% | 6 | 15 | 0 | 16 |
| 42.93915647 | 22.7% | 100.0% | 5 | 15 | 0 | 17 |
| 44.44568121 | 18.2% | 100.0% | 4 | 15 | 0 | 18 |
| 44.51626947 | 13.6% | 100.0% | 3 | 15 | 0 | 19 |
| 95.0004203 | 9.1% | 100.0% | 2 | 15 | 0 | 20 |
| 141.0738233 | 4.5% | 100.0% | 1 | 15 | 0 | 21 |
| 3147.932227 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

Test Receiver Operator Characteristic (ROC) curves

M7092_76 by SAMP_GRP

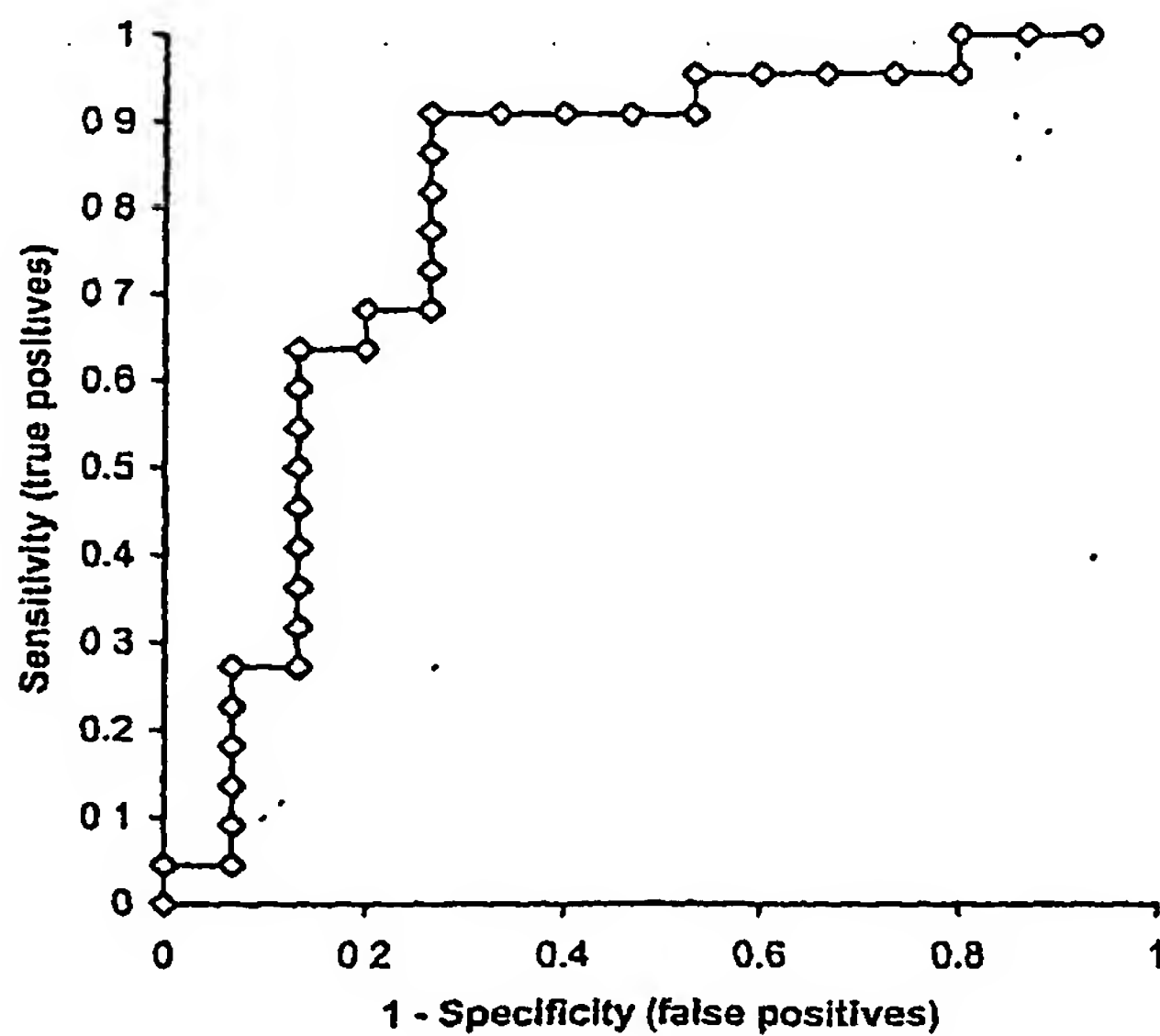
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|---------|----------------|--------------------|
| M7092_76 | 0.806 | 0.0814 | <0.0001 | 0.647 to 0.966 | have higher values |



| M7092_76
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 0.116985513 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

Test Receiver Operator Characteristic (ROC) curves

M7092_76 by SAMP_GRP

| Performed by | Date | | | | | |
|--------------|--------|--------|----|----|----|----|
| 1.862910226 | 100.0% | 13.3% | 22 | 2 | 13 | 0 |
| 2.957763417 | 100.0% | 20.0% | 22 | 3 | 12 | 0 |
| 3.222148121 | 95.5% | 20.0% | 21 | 3 | 12 | 1 |
| 3.27231959 | 95.5% | 26.7% | 21 | 4 | 11 | 1 |
| 3.282820708 | 95.5% | 33.3% | 21 | 5 | 10 | 1 |
| 4.001971072 | 95.5% | 40.0% | 21 | 6 | 9 | 1 |
| 4.04949334 | 95.5% | 46.7% | 21 | 7 | 8 | 1 |
| 4.153630114 | 90.9% | 46.7% | 20 | 7 | 8 | 2 |
| 4.497343511 | 90.9% | 53.3% | 20 | 8 | 7 | 2 |
| 4.918339938 | 90.9% | 60.0% | 20 | 9 | 6 | 2 |
| 5.151284095 | 90.9% | 66.7% | 20 | 10 | 5 | 2 |
| 5.334167589 | 90.9% | 73.3% | 20 | 11 | 4 | 2 |
| 5.552935622 | 86.4% | 73.3% | 19 | 11 | 4 | 3 |
| 5.901348367 | 81.8% | 73.3% | 18 | 11 | 4 | 4 |
| 6.449491292 | 77.3% | 73.3% | 17 | 11 | 4 | 5 |
| 8.769308501 | 72.7% | 73.3% | 16 | 11 | 4 | 6 |
| 8.803059652 | 68.2% | 73.3% | 15 | 11 | 4 | 7 |
| 8.919510428 | 68.2% | 80.0% | 15 | 12 | 3 | 7 |
| 10.19427001 | 63.6% | 80.0% | 14 | 12 | 3 | 8 |
| 10.45580495 | 63.6% | 86.7% | 14 | 13 | 2 | 8 |
| 12.59614789 | 59.1% | 86.7% | 13 | 13 | 2 | 9 |
| 16.83451689 | 54.5% | 86.7% | 12 | 13 | 2 | 10 |
| 22.00466543 | 50.0% | 86.7% | 11 | 13 | 2 | 11 |
| 23.47247801 | 45.5% | 86.7% | 10 | 13 | 2 | 12 |
| 26.17734222 | 40.9% | 86.7% | 9 | 13 | 2 | 13 |
| 27.02830203 | 36.4% | 86.7% | 8 | 13 | 2 | 14 |
| 29.83138707 | 31.8% | 86.7% | 7 | 13 | 2 | 15 |
| 39.98526477 | 27.3% | 86.7% | 6 | 13 | 2 | 16 |
| 44.65059349 | 27.3% | 93.3% | 6 | 14 | 1 | 16 |
| 46.65430614 | 22.7% | 93.3% | 5 | 14 | 1 | 17 |
| 54.13737253 | 18.2% | 93.3% | 4 | 14 | 1 | 18 |
| 100.3851762 | 13.6% | 93.3% | 3 | 14 | 1 | 19 |
| 110.8760403 | 9.1% | 93.3% | 2 | 14 | 1 | 20 |
| 153.059446 | 4.5% | 93.3% | 1 | 14 | 1 | 21 |
| 168.4616351 | 4.5% | 100.0% | 1 | 15 | 0 | 21 |
| 426.5909767 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

7.3.10

analysed with Analyse-it + Clinical Laboratory 1 62

Test Receiver Operator Characteristic (ROC) curves

M7314_17 by SAMP_GRP

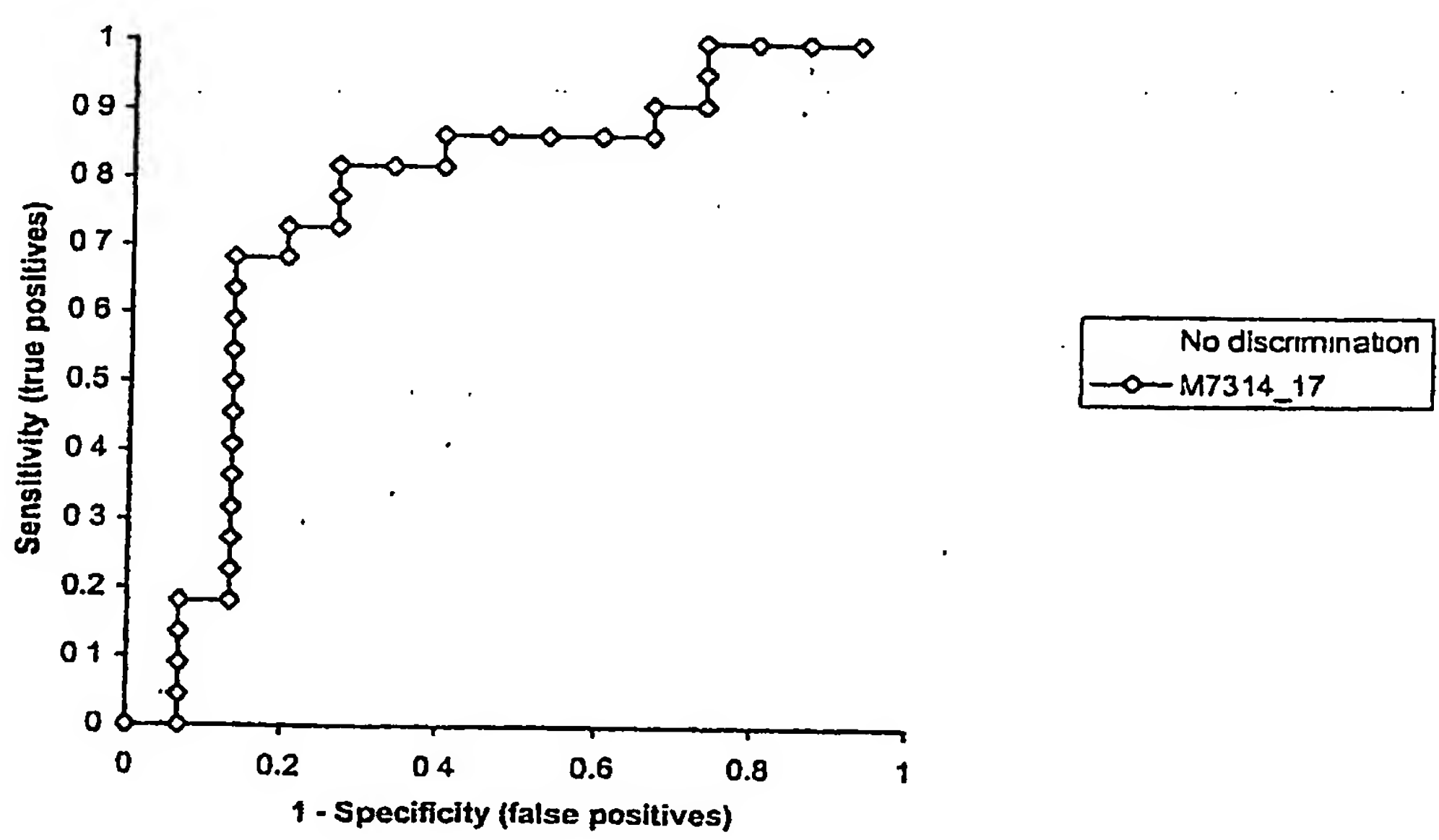
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M7314_17 | 0.773 | 0.0867 | 0.0008 | 0.603 to 0.943 | have higher values |



| M7314_17
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 1.114997332 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

Test Receiver Operator Characteristic (ROC) curves

M7314_17 by SAMP_GRP

| Performed by | Date | | | | | |
|--------------|--------|--------|----|----|----|----|
| 1.180169107 | 100.0% | 13.3% | 22 | 2 | 13 | 0 |
| 1.224623102 | 100.0% | 20.0% | 22 | 3 | 12 | 0 |
| 1.326553822 | 100.0% | 26.7% | 22 | 4 | 11 | 0 |
| 1.709052162 | 95.5% | 26.7% | 21 | 4 | 11 | 1 |
| 1.77348404 | 90.9% | 26.7% | 20 | 4 | 11 | 2 |
| 2.236875714 | 90.9% | 33.3% | 20 | 5 | 10 | 2 |
| 2.240777654 | 86.4% | 33.3% | 19 | 5 | 10 | 3 |
| 2.352830697 | 86.4% | 40.0% | 19 | 6 | 9 | 3 |
| 2.475113163 | 86.4% | 46.7% | 19 | 7 | 8 | 3 |
| 2.834024541 | 86.4% | 53.3% | 19 | 8 | 7 | 3 |
| 2.919756862 | 86.4% | 60.0% | 19 | 9 | 6 | 3 |
| 2.964311998 | 81.8% | 60.0% | 18 | 9 | 6 | 4 |
| 2.98055665 | 81.8% | 66.7% | 18 | 10 | 5 | 4 |
| 3.310074994 | 81.8% | 73.3% | 18 | 11 | 4 | 4 |
| 3.873756225 | 77.3% | 73.3% | 17 | 11 | 4 | 5 |
| 5.048148574 | 72.7% | 73.3% | 16 | 11 | 4 | 6 |
| 5.051833408 | 72.7% | 80.0% | 16 | 12 | 3 | 6 |
| 6.248643692 | 68.2% | 80.0% | 15 | 12 | 3 | 7 |
| 6.682066684 | 68.2% | 86.7% | 15 | 13 | 2 | 7 |
| 8.598671796 | 63.6% | 86.7% | 14 | 13 | 2 | 8 |
| 9.39521205 | 59.1% | 86.7% | 13 | 13 | 2 | 9 |
| 10.56821695 | 54.5% | 86.7% | 12 | 13 | 2 | 10 |
| 13.53952374 | 50.0% | 86.7% | 11 | 13 | 2 | 11 |
| 14.17616623 | 45.5% | 86.7% | 10 | 13 | 2 | 12 |
| 15.60825923 | 40.9% | 86.7% | 9 | 13 | 2 | 13 |
| 17.90393685 | 36.4% | 86.7% | 8 | 13 | 2 | 14 |
| 19.91147186 | 31.8% | 86.7% | 7 | 13 | 2 | 15 |
| 25.18734431 | 27.3% | 86.7% | 6 | 13 | 2 | 16 |
| 27.36118714 | 22.7% | 86.7% | 5 | 13 | 2 | 17 |
| 32.78098195 | 18.2% | 86.7% | 4 | 13 | 2 | 18 |
| 34.78889153 | 18.2% | 93.3% | 4 | 14 | 1 | 18 |
| 43.45506451 | 13.6% | 93.3% | 3 | 14 | 1 | 19 |
| 59.53332127 | 9.1% | 93.3% | 2 | 14 | 1 | 20 |
| 63.66042898 | 4.5% | 93.3% | 1 | 14 | 1 | 21 |
| 69.34508241 | 0.0% | 93.3% | 0 | 14 | 1 | 22 |
| 73.87428099 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

7.2 WD

analysed with Analyse-it + Clinical Laboratory 1 62

Test Receiver Operator Characteristic (ROC) curves

M7512_62 by SAMP_GRP

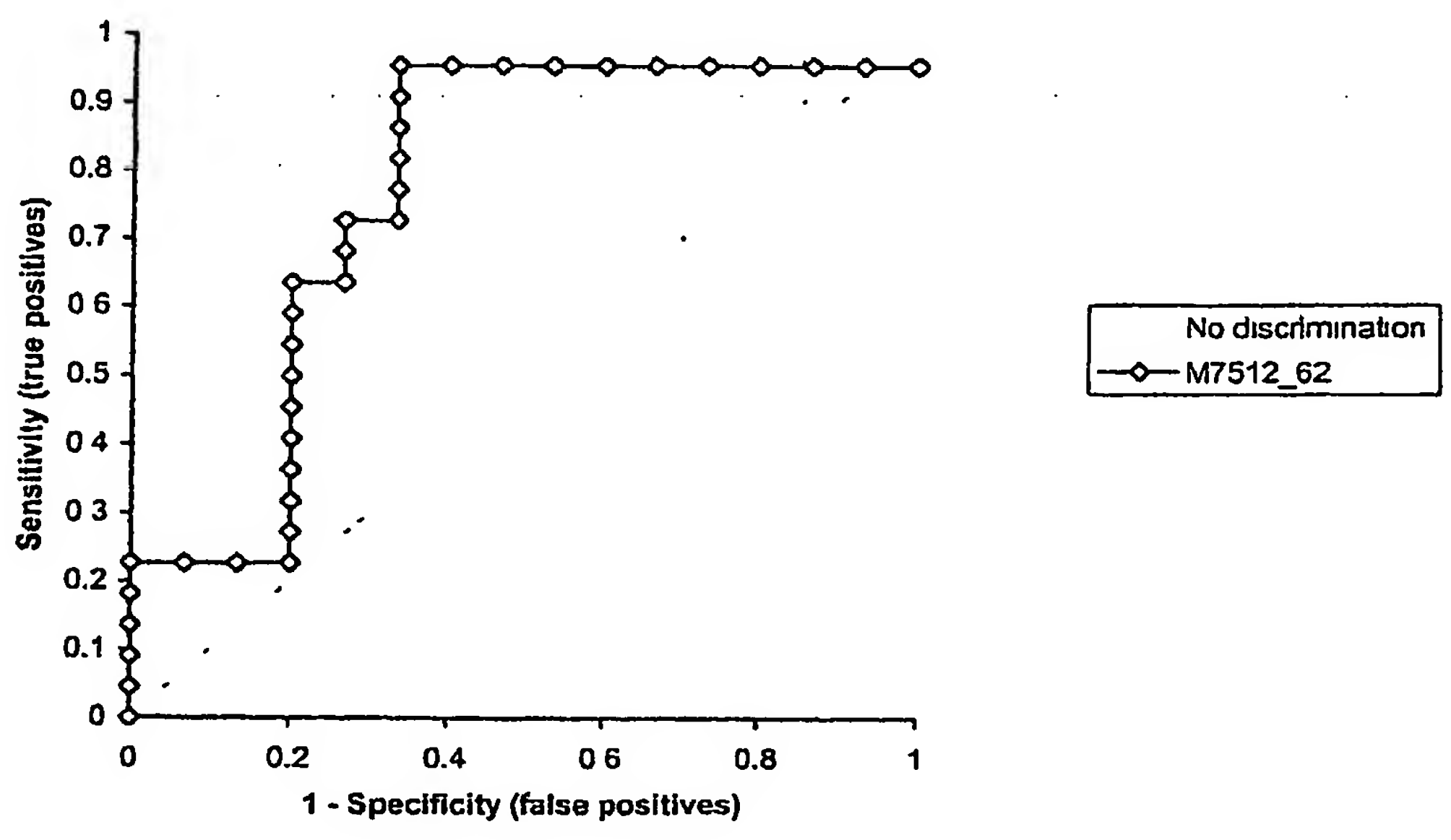
Performed by

Date

n 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M7512_62 | 0.773 | 0.0871 | 0.0009 | 0.602 to 0.943 | have higher values |



| M7512_62
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 0.625410695 | 95.5% | 0.0% | 21 | 0 | 15 | 1 |

Test Receiver Operator Characteristic (ROC) curves

M7512_62 by SAMP_GRP

| Performed by | | | | | Date | |
|--------------|-------|--------|----|----|------|----|
| 0.762104663 | 95.5% | 6.7% | 21 | 1 | 14 | 1 |
| 1.122272393 | 95.5% | 13.3% | 21 | 2 | 13 | 1 |
| 1.378372019 | 95.5% | 20.0% | 21 | 3 | 12 | 1 |
| 1.546262948 | 95.5% | 26.7% | 21 | 4 | 11 | 1 |
| 1.643886277 | 95.5% | 33.3% | 21 | 5 | 10 | 1 |
| 1.661108564 | 95.5% | 40.0% | 21 | 6 | 9 | 1 |
| 3.058893486 | 95.5% | 46.7% | 21 | 7 | 8 | 1 |
| 3.78575016 | 95.5% | 53.3% | 21 | 8 | 7 | 1 |
| 3.846409634 | 95.5% | 60.0% | 21 | 9 | 6 | 1 |
| 3.907858158 | 95.5% | 66.7% | 21 | 10 | 5 | 1 |
| 4.753500925 | 90.9% | 66.7% | 20 | 10 | 5 | 2 |
| 4.94581107 | 86.4% | 66.7% | 19 | 10 | 5 | 3 |
| 5.833371244 | 81.8% | 66.7% | 18 | 10 | 5 | 4 |
| 5.872789172 | 77.3% | 66.7% | 17 | 10 | 5 | 5 |
| 5.879481156 | 72.7% | 66.7% | 16 | 10 | 5 | 6 |
| 6.660721221 | 72.7% | 73.3% | 16 | 11 | 4 | 6 |
| 7.500832279 | 68.2% | 73.3% | 15 | 11 | 4 | 7 |
| 7.675599479 | 63.6% | 73.3% | 14 | 11 | 4 | 8 |
| 7.972317528 | 63.6% | 80.0% | 14 | 12 | 3 | 8 |
| 10.66838021 | 59.1% | 80.0% | 13 | 12 | 3 | 9 |
| 11.59554514 | 54.5% | 80.0% | 12 | 12 | 3 | 10 |
| 12.97571036 | 50.0% | 80.0% | 11 | 12 | 3 | 11 |
| 14.88590508 | 45.5% | 80.0% | 10 | 12 | 3 | 12 |
| 17.39851187 | 40.9% | 80.0% | 9 | 12 | 3 | 13 |
| 20.28527567 | 36.4% | 80.0% | 8 | 12 | 3 | 14 |
| 21.55862835 | 31.8% | 80.0% | 7 | 12 | 3 | 15 |
| 24.05640739 | 27.3% | 80.0% | 6 | 12 | 3 | 16 |
| 25.55057933 | 22.7% | 80.0% | 5 | 12 | 3 | 17 |
| 25.57183388 | 22.7% | 86.7% | 5 | 13 | 2 | 17 |
| 28.47338716 | 22.7% | 93.3% | 5 | 14 | 1 | 17 |
| 31.73736348 | 22.7% | 100.0% | 5 | 15 | 0 | 17 |
| 51.03701678 | 18.2% | 100.0% | 4 | 15 | 0 | 18 |
| 55.37243893 | 13.6% | 100.0% | 3 | 15 | 0 | 19 |
| 91.83881699 | 9.1% | 100.0% | 2 | 15 | 0 | 20 |
| 126.9859246 | 4.5% | 100.0% | 1 | 15 | 0 | 21 |
| 165.9115088 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

Test | Receiver Operator Characteristic (ROC) curves

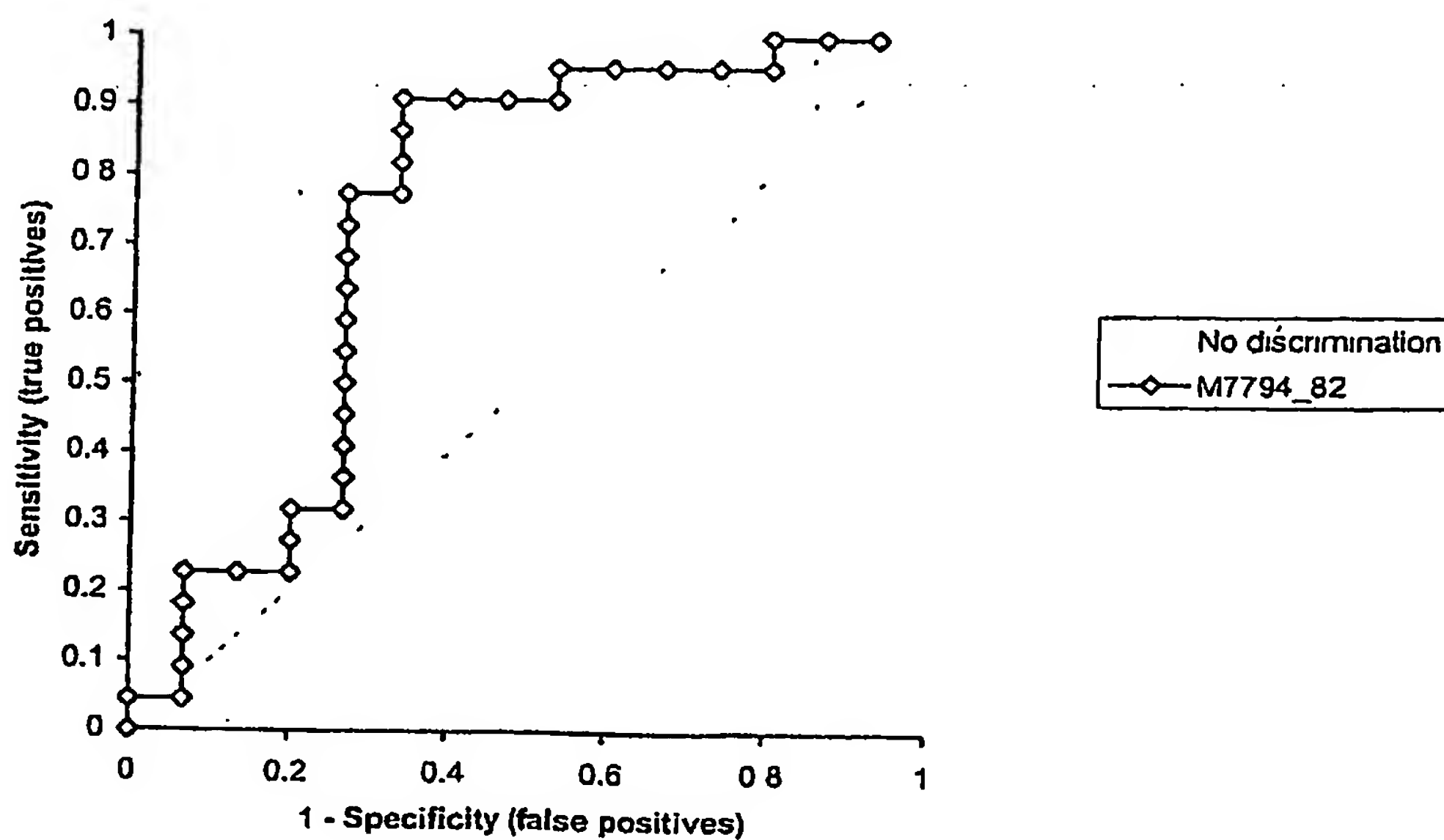
Performed by

Date _____

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M7794_82 | 0.742 | 0.0938 | 0.0049 | 0.559 to 0.926 | have higher values |



| M7794_82
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| -0.08627241 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

Test Receiver Operator Characteristic (ROC) curves

M7794_82 by SAMP_GRP

| Performed by | | | | | | Date | |
|--------------|--------|--------|----|----|----|------|--|
| 0.013815951 | 100.0% | 13.3% | 22 | 2 | 13 | 0 | |
| 0.049455599 | 100.0% | 20.0% | 22 | 3 | 12 | 0 | |
| 0.095260382 | 95.5% | 20.0% | 21 | 3 | 12 | 1 | |
| 0.109513792 | 95.5% | 26.7% | 21 | 4 | 11 | 1 | |
| 0.186117689 | 95.5% | 33.3% | 21 | 5 | 10 | 1 | |
| 0.402645583 | 95.5% | 40.0% | 21 | 6 | 9 | 1 | |
| 0.452914233 | 95.5% | 46.7% | 21 | 7 | 8 | 1 | |
| 0.484984253 | 90.9% | 46.7% | 20 | 7 | 8 | 2 | |
| 0.536323113 | 90.9% | 53.3% | 20 | 8 | 7 | 2 | |
| 0.563391393 | 90.9% | 60.0% | 20 | 9 | 6 | 2 | |
| 0.693832415 | 90.9% | 66.7% | 20 | 10 | 5 | 2 | |
| 0.765652442 | 86.4% | 66.7% | 19 | 10 | 5 | 3 | |
| 0.783555475 | 81.8% | 66.7% | 18 | 10 | 5 | 4 | |
| 0.858183653 | 77.3% | 66.7% | 17 | 10 | 5 | 5 | |
| 0.888201349 | 77.3% | 73.3% | 17 | 11 | 4 | 5 | |
| 0.902269861 | 72.7% | 73.3% | 16 | 11 | 4 | 6 | |
| 0.908749925 | 68.2% | 73.3% | 15 | 11 | 4 | 7 | |
| 0.954138409 | 63.6% | 73.3% | 14 | 11 | 4 | 8 | |
| 0.956932268 | 59.1% | 73.3% | 13 | 11 | 4 | 9 | |
| 1.040190836 | 54.5% | 73.3% | 12 | 11 | 4 | 10 | |
| 1.38805676 | 50.0% | 73.3% | 11 | 11 | 4 | 11 | |
| 1.462958498 | 45.5% | 73.3% | 10 | 11 | 4 | 12 | |
| 1.565809169 | 40.9% | 73.3% | 9 | 11 | 4 | 13 | |
| 1.639589588 | 36.4% | 73.3% | 8 | 11 | 4 | 14 | |
| 1.659493689 | 31.8% | 73.3% | 7 | 11 | 4 | 15 | |
| 1.797384017 | 31.8% | 80.0% | 7 | 12 | 3 | 15 | |
| 1.821160291 | 27.3% | 80.0% | 6 | 12 | 3 | 16 | |
| 1.958973143 | 22.7% | 80.0% | 5 | 12 | 3 | 17 | |
| 2.138566227 | 22.7% | 86.7% | 5 | 13 | 2 | 17 | |
| 2.14742124 | 22.7% | 93.3% | 5 | 14 | 1 | 17 | |
| 2.880841629 | 18.2% | 93.3% | 4 | 14 | 1 | 18 | |
| 3.76104205 | 13.6% | 93.3% | 3 | 14 | 1 | 19 | |
| 5.412710799 | 9.1% | 93.3% | 2 | 14 | 1 | 20 | |
| 11.82552702 | 4.5% | 93.3% | 1 | 14 | 1 | 21 | |
| 23.67610979 | 4.5% | 100.0% | 1 | 15 | 0 | 21 | |
| 44.68965421 | 0.0% | 100.0% | 0 | 15 | 0 | 22 | |

B.D WP

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analysed with: Analyse-It + Clinical Laboratory 1 62

Test Receiver Operator Characteristic (ROC) curves

M8008_80 by SAMP_GRP

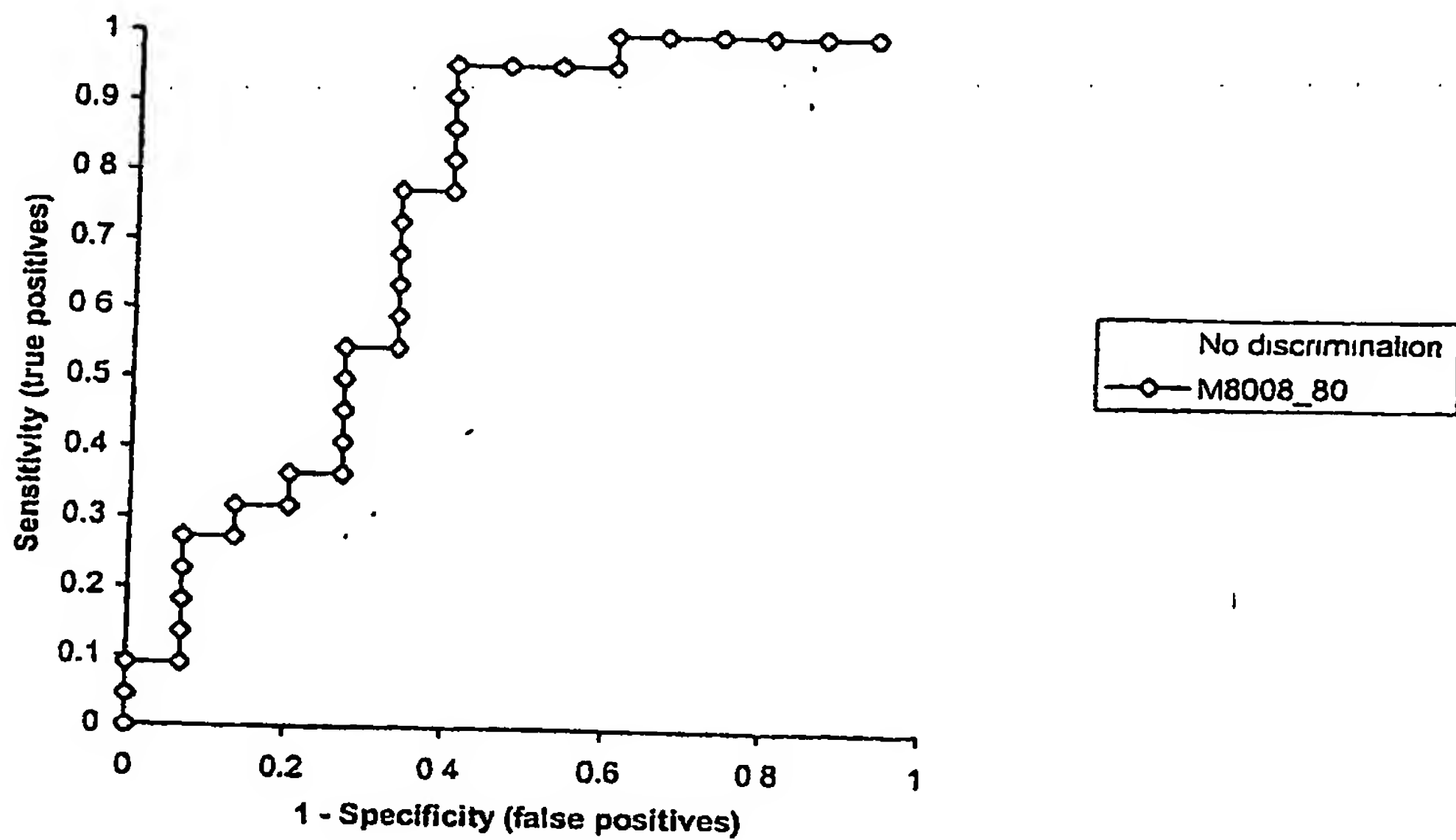
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M8008_80 | 0.748 | 0.0901 | 0.0029 | 0.572 to 0.925 | have higher values |



| M8008_80
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 1.11982771 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

M8008_80 by SAMP_GRP

| Performed by | | | | | Date | |
|--------------|--------|--------|----|----|------|----|
| 1.359759553 | 100.0% | 13.3% | 22 | 2 | 13 | 0 |
| 2.654253558 | 100.0% | 20.0% | 22 | 3 | 12 | 0 |
| 2.808461046 | 100.0% | 26.7% | 22 | 4 | 11 | 0 |
| 3.26845117 | 100.0% | 33.3% | 22 | 5 | 10 | 0 |
| 3.528811365 | 100 0% | 40.0% | 22 | 6 | 9 | 0 |
| 3.536888491 | 95.5% | 40.0% | 21 | 6 | 9 | 1 |
| 3.690604924 | 95.5% | 46.7% | 21 | 7 | 8 | 1 |
| 3.846135566 | 95.5% | 53.3% | 21 | 8 | 7 | 1 |
| 4.063516487 | 95.5% | 60.0% | 21 | 9 | 6 | 1 |
| 4.968072731 | 90.9% | 60.0% | 20 | 9 | 6 | 2 |
| 5.11309322 | 86.4% | 60.0% | 19 | 9 | 6 | 3 |
| 5.244061045 | 81.8% | 60.0% | 18 | 9 | 6 | 4 |
| 5.519460219 | 77 3% | 60.0% | 17 | 9 | 6 | 5 |
| 5.746787228 | 77.3% | 66.7% | 17 | 10 | 5 | 5 |
| 5.888803285 | 72.7% | 66.7% | 16 | 10 | 5 | 6 |
| 6.029356242 | 68.2% | 66.7% | 15 | 10 | 5 | 7 |
| 6.808604885 | 63.6% | 66.7% | 14 | 10 | 5 | 8 |
| 7.221723174 | 59.1% | 66.7% | 13 | 10 | 5 | 9 |
| 9.085606959 | 54 5% | 66 7% | 12 | 10 | 5 | 10 |
| 9.917829533 | 54.5% | 73.3% | 12 | 11 | 4 | 10 |
| 9.97218851 | 50 0% | 73.3% | 11 | 11 | 4 | 11 |
| 11.13193439 | 45.5% | 73.3% | 10 | 11 | 4 | 12 |
| 12.52006708 | 40.9% | 73.3% | 9 | 11 | 4 | 13 |
| 14.11770896 | 36 4% | 73.3% | 8 | 11 | 4 | 14 |
| 14.2002752 | 36.4% | 80 0% | 8 | 12 | 3 | 14 |
| 14.48384235 | 31.8% | 80.0% | 7 | 12 | 3 | 15 |
| 14.97244447 | 31.8% | 86.7% | 7 | 13 | 2 | 15 |
| 22.61737089 | 27 3% | 86.7% | 6 | 13 | 2 | 16 |
| 22.63182262 | 27.3% | 93.3% | 6 | 14 | 1 | 16 |
| 36.86081226 | 22.7% | 93.3% | 5 | 14 | 1 | 17 |
| 44.85462631 | 18.2% | 93.3% | 4 | 14 | 1 | 18 |
| 45.65159336 | 13.6% | 93.3% | 3 | 14 | 1 | 19 |
| 57.40336361 | 9.1% | 93.3% | 2 | 14 | 1 | 20 |
| 71.56935595 | 9.1% | 100.0% | 2 | 15 | 0 | 20 |
| 80.11117489 | 4.5% | 100.0% | 1 | 15 | 0 | 21 |
| 85.83353633 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

B.1 KD

Test Receiver Operator Characteristic (ROC) curves

analysed with Analyse-It + Clinical Laboratory 1 62

M8126_49 by SAMP_GRP

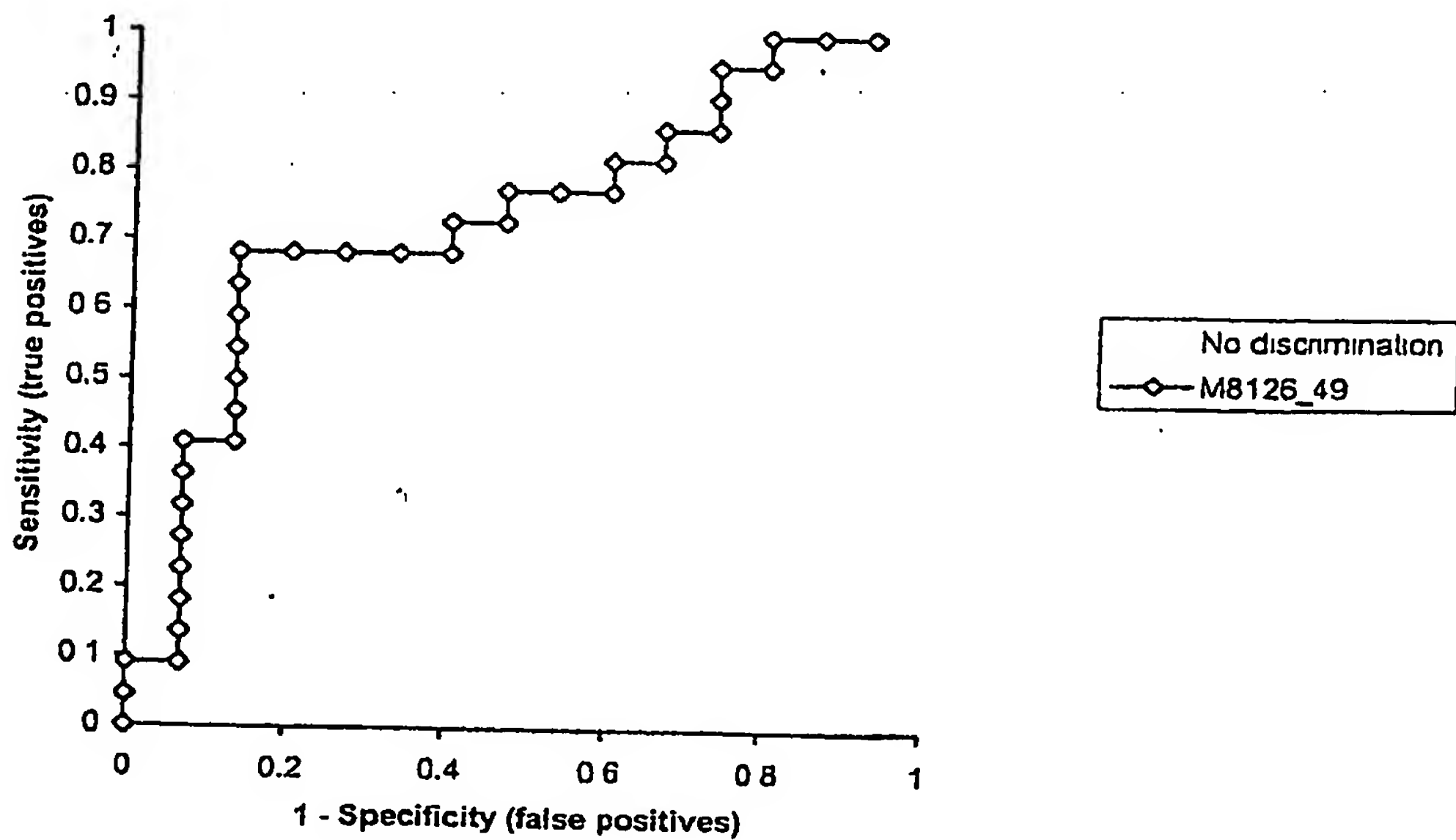
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M8126_49 | 0.742 | 0.0842 | 0.0020 | 0.577 to 0.907 | have higher values |



| M8126_49
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| -0.242649757 | 100 0% | 6.7% | 22 | 1 | 14 | 0 |

Test Receiver Operator Characteristic (ROC) curves

M8126_49 by SAMP_GRP

| Performed by | | | | | Date | |
|--------------|--------|--------|----|----|------|----|
| 0.530442832 | 100.0% | 13.3% | 22 | 2 | 13 | 0 |
| 0.644223404 | 100.0% | 20.0% | 22 | 3 | 12 | 0 |
| 0.885640373 | 95.5% | 20.0% | 21 | 3 | 12 | 1 |
| 1.433559793 | 95.5% | 26.7% | 21 | 4 | 11 | 1 |
| 1.794431151 | 90.9% | 26.7% | 20 | 4 | 11 | 2 |
| 1.818318183 | 86.4% | 26.7% | 19 | 4 | 11 | 3 |
| 2.079303745 | 86.4% | 33.3% | 19 | 5 | 10 | 3 |
| 2.114695472 | 81.8% | 33.3% | 18 | 5 | 10 | 4 |
| 2.300483675 | 81.8% | 40.0% | 18 | 6 | 9 | 4 |
| 2.557169627 | 77.3% | 40.0% | 17 | 6 | 9 | 5 |
| 2.691146289 | 77.3% | 46.7% | 17 | 7 | 8 | 5 |
| 2.8048776 | 77.3% | 53.3% | 17 | 8 | 7 | 5 |
| 2.971536888 | 72.7% | 53.3% | 16 | 8 | 7 | 6 |
| 3.295574013 | 72.7% | 60.0% | 16 | 9 | 6 | 6 |
| 3.625766621 | 68.2% | 60.0% | 15 | 9 | 6 | 7 |
| 3.644660813 | 68.2% | 66.7% | 15 | 10 | 5 | 7 |
| 3.736933608 | 68.2% | 73.3% | 15 | 11 | 4 | 7 |
| 3.737652044 | 68.2% | 80.0% | 15 | 12 | 3 | 7 |
| 3.79710601 | 68.2% | 86.7% | 15 | 13 | 2 | 7 |
| 3.806135483 | 63.6% | 86.7% | 14 | 13 | 2 | 8 |
| 4.042986903 | 59.1% | 86.7% | 13 | 13 | 2 | 9 |
| 4.074173818 | 54.5% | 86.7% | 12 | 13 | 2 | 10 |
| 4.688852396 | 50.0% | 86.7% | 11 | 13 | 2 | 11 |
| 4.796496576 | 45.5% | 86.7% | 10 | 13 | 2 | 12 |
| 4.965020089 | 40.9% | 86.7% | 9 | 13 | 2 | 13 |
| 5.066333812 | 40.9% | 93.3% | 9 | 14 | 1 | 13 |
| 5.576272551 | 36.4% | 93.3% | 8 | 14 | 1 | 14 |
| 6.491330575 | 31.8% | 93.3% | 7 | 14 | 1 | 15 |
| 6.795353009 | 27.3% | 93.3% | 6 | 14 | 1 | 16 |
| 7.076142913 | 22.7% | 93.3% | 5 | 14 | 1 | 17 |
| 22.76210615 | 18.2% | 93.3% | 4 | 14 | 1 | 18 |
| 25.8590526 | 13.6% | 93.3% | 3 | 14 | 1 | 19 |
| 28.51064176 | 9.1% | 93.3% | 2 | 14 | 1 | 20 |
| 42.61452812 | 9.1% | 100.0% | 2 | 15 | 0 | 20 |
| 65.64727304 | 4.5% | 100.0% | 1 | 15 | 0 | 21 |
| 129.1652158 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

9,10 WD

analysed with Analyse-it + Clinical Laboratory 1 62

Test Receiver Operator Characteristic (ROC) curves

M9032_41 by SAMP_GRP

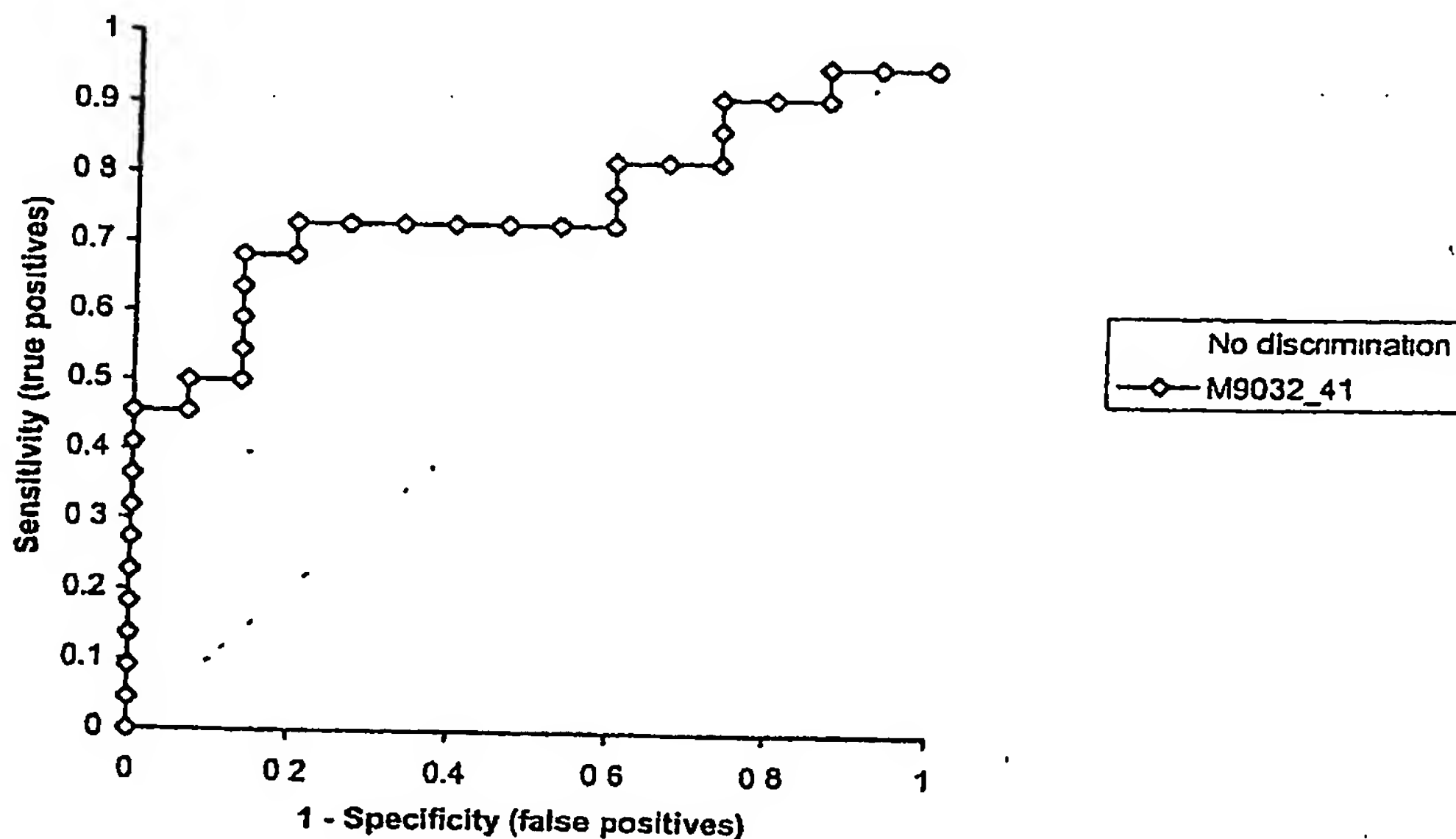
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|-------------------|
| M9032_41 | 0.758 | 0.0800 | 0.0006 | 0.601 to 0.914 | have lower values |



| M9032_41
(abnormals below cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 0.301214127 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

Test Receiver Operator Characteristic (ROC) curves

M9032_41 by SAMP_GRP

| Performed by | | | | | Date | |
|--------------|-------|--------|----|----|------|----|
| 0.803405811 | 4.5% | 100.0% | 1 | 15 | 0 | 21 |
| 0.998249125 | 9.1% | 100.0% | 2 | 15 | 0 | 20 |
| 1.176635111 | 13.6% | 100.0% | 3 | 15 | 0 | 19 |
| 1.292732389 | 18.2% | 100.0% | 4 | 15 | 0 | 18 |
| 1.37399724 | 22.7% | 100.0% | 5 | 15 | 0 | 17 |
| 1.374238023 | 27.3% | 100.0% | 6 | 15 | 0 | 16 |
| 1.469324005 | 31.8% | 100.0% | 7 | 15 | 0 | 15 |
| 1.495648575 | 36.4% | 100.0% | 8 | 15 | 0 | 14 |
| 1.666667202 | 40.9% | 100.0% | 9 | 15 | 0 | 13 |
| 1.712649617 | 45.5% | 100.0% | 10 | 15 | 0 | 12 |
| 1.920543547 | 45.5% | 93.3% | 10 | 14 | 1 | 12 |
| 2.133352538 | 50.0% | 93.3% | 11 | 14 | 1 | 11 |
| 2.28590313 | 50.0% | 86.7% | 11 | 13 | 2 | 11 |
| 2.329098269 | 54.5% | 86.7% | 12 | 13 | 2 | 10 |
| 2.490115349 | 59.1% | 86.7% | 13 | 13 | 2 | 9 |
| 2.562278576 | 63.6% | 86.7% | 14 | 13 | 2 | 8 |
| 2.924448973 | 68.2% | 86.7% | 15 | 13 | 2 | 7 |
| 3.201543343 | 68.2% | 80.0% | 15 | 12 | 3 | 7 |
| 3.24060916 | 72.7% | 80.0% | 16 | 12 | 3 | 6 |
| 4.080807466 | 72.7% | 73.3% | 16 | 11 | 4 | 6 |
| 4.120817587 | 72.7% | 66.7% | 16 | 10 | 5 | 6 |
| 4.392505873 | 72.7% | 60.0% | 16 | 9 | 6 | 6 |
| 4.794477164 | 72.7% | 53.3% | 16 | 8 | 7 | 6 |
| 4.79606144 | 72.7% | 46.7% | 16 | 7 | 8 | 6 |
| 5.425100163 | 72.7% | 40.0% | 16 | 6 | 9 | 6 |
| 5.938344901 | 77.3% | 40.0% | 17 | 6 | 9 | 5 |
| 6.31378122 | 81.8% | 40.0% | 18 | 6 | 9 | 4 |
| 6.591704626 | 81.8% | 33.3% | 18 | 5 | 10 | 4 |
| 8.267892434 | 81.8% | 26.7% | 18 | 4 | 11 | 4 |
| 8.671042606 | 86.4% | 26.7% | 19 | 4 | 11 | 3 |
| 10.61510852 | 90.9% | 26.7% | 20 | 4 | 11 | 2 |
| 12.72350271 | 90.9% | 20.0% | 20 | 3 | 12 | 2 |
| 13.23403263 | 90.9% | 13.3% | 20 | 2 | 13 | 2 |
| 23.24713623 | 95.5% | 13.3% | 21 | 2 | 13 | 1 |
| 30.65382604 | 95.5% | 6.7% | 21 | 1 | 14 | 1 |
| 90.70489507 | 95.5% | 0.0% | 21 | 0 | 15 | 1 |

9.1KD

analysed with Analyse-it + Clinical Laboratory 1.6

Test Receiver Operator Characteristic (ROC) curves

M9134_84 by SAMP_GRP

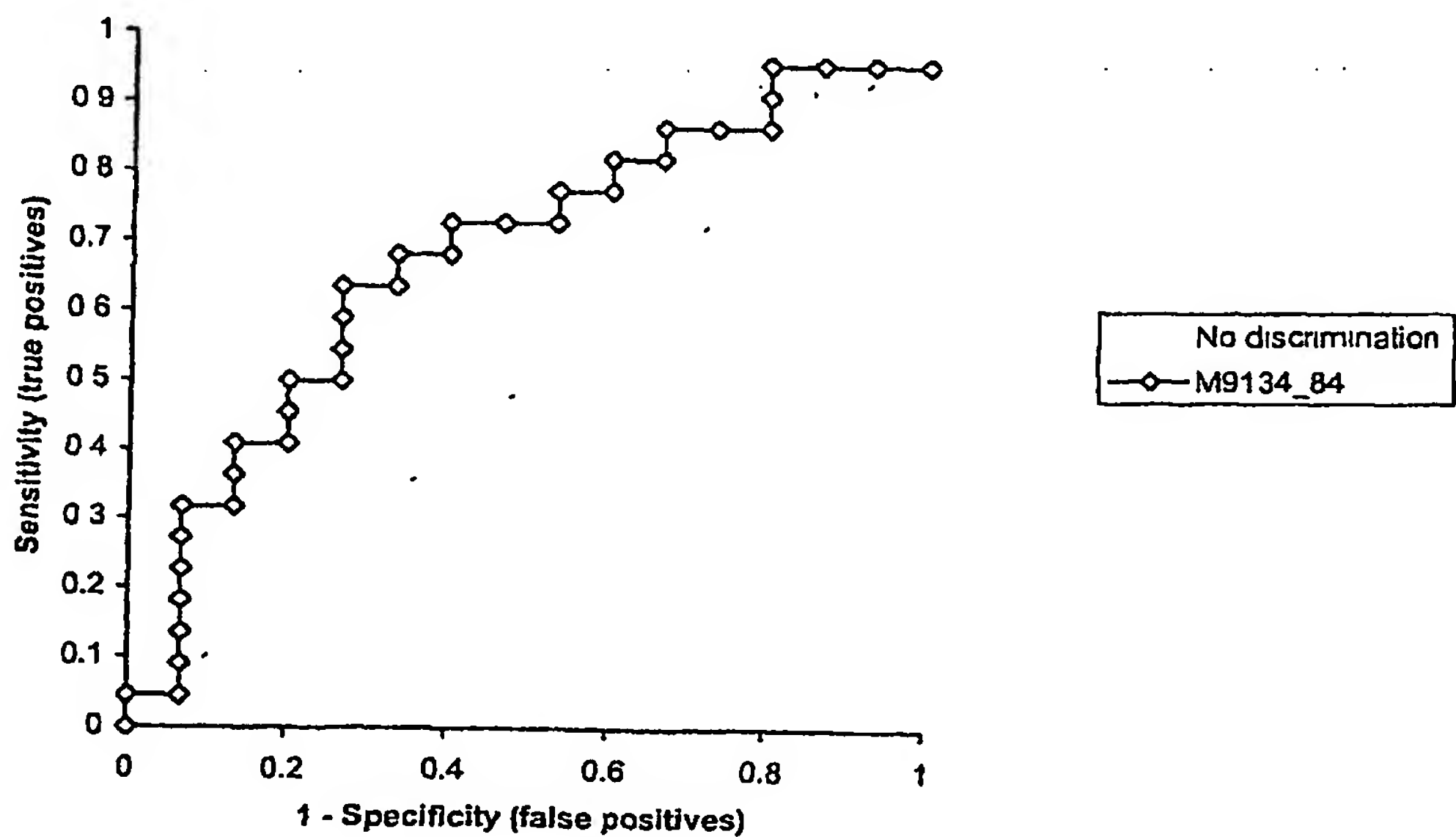
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|-------------------|
| M9134_84 | 0.682 | 0.0904 | 0.0221 | 0.505 to 0.859 | have lower values |



| M9134_84
(abnormals below cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| -0.230457138 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

Test Receiver Operator Characteristic (ROC) curves

M9134_84 by SAMP_GRP

| Performed by | | | | | Date | |
|--------------|-------|--------|----|----|------|----|
| 0.303716546 | 4.5% | 100.0% | 1 | 15 | 0 | 21 |
| 0.422909754 | 4.5% | 93.3% | 1 | 14 | 1 | 21 |
| 0.679789975 | 9.1% | 93.3% | 2 | 14 | 1 | 20 |
| 1.15660303 | 13.6% | 93.3% | 3 | 14 | 1 | 19 |
| 1.185904471 | 18.2% | 93.3% | 4 | 14 | 1 | 18 |
| 1.247739984 | 22.7% | 93.3% | 5 | 14 | 1 | 17 |
| 1.284010996 | 27.3% | 93.3% | 6 | 14 | 1 | 16 |
| 1.37596149 | 31.8% | 93.3% | 7 | 14 | 1 | 15 |
| 1.576186258 | 31.8% | 86.7% | 7 | 13 | 2 | 15 |
| 1.851196687 | 36.4% | 86.7% | 8 | 13 | 2 | 14 |
| 1.878772545 | 40.9% | 86.7% | 9 | 13 | 2 | 13 |
| 1.897908011 | 40.9% | 80.0% | 9 | 12 | 3 | 13 |
| 2.290261208 | 45.5% | 80.0% | 10 | 12 | 3 | 12 |
| 2.575036839 | 50.0% | 80.0% | 11 | 12 | 3 | 11 |
| 2.580613336 | 50.0% | 73.3% | 11 | 11 | 4 | 11 |
| 2.736807216 | 54.5% | 73.3% | 12 | 11 | 4 | 10 |
| 2.812866946 | 59.1% | 73.3% | 13 | 11 | 4 | 9 |
| 2.878357233 | 63.6% | 73.3% | 14 | 11 | 4 | 8 |
| 3.489262381 | 63.6% | 66.7% | 14 | 10 | 5 | 8 |
| 3.739002718 | 68.2% | 66.7% | 15 | 10 | 5 | 7 |
| 4.129794763 | 68.2% | 60.0% | 15 | 9 | 6 | 7 |
| 4.256950328 | 72.7% | 60.0% | 16 | 9 | 6 | 6 |
| 4.378021704 | 72.7% | 53.3% | 16 | 8 | 7 | 6 |
| 4.389813191 | 72.7% | 46.7% | 16 | 7 | 8 | 6 |
| 4.775583174 | 77.3% | 46.7% | 17 | 7 | 8 | 5 |
| 6.554049654 | 77.3% | 40.0% | 17 | 6 | 9 | 5 |
| 6.738969207 | 81.8% | 40.0% | 18 | 6 | 9 | 4 |
| 7.172153745 | 81.8% | 33.3% | 18 | 5 | 10 | 4 |
| 7.571982855 | 86.4% | 33.3% | 19 | 5 | 10 | 3 |
| 8.817682331 | 86.4% | 26.7% | 19 | 4 | 11 | 3 |
| 14.6752361 | 86.4% | 20.0% | 19 | 3 | 12 | 3 |
| 15.48975496 | 90.9% | 20.0% | 20 | 3 | 12 | 2 |
| 15.79923578 | 95.5% | 20.0% | 21 | 3 | 12 | 1 |
| 17.61892743 | 95.5% | 13.3% | 21 | 2 | 13 | 1 |
| 30.84421482 | 95.5% | 6.7% | 21 | 1 | 14 | 1 |
| 89.35626416 | 95.5% | 0.0% | 21 | 0 | 15 | 1 |

G.3 WD

Test Receiver Operator Characteristic (ROC) curves

M9259_73 by SAMP_GRP

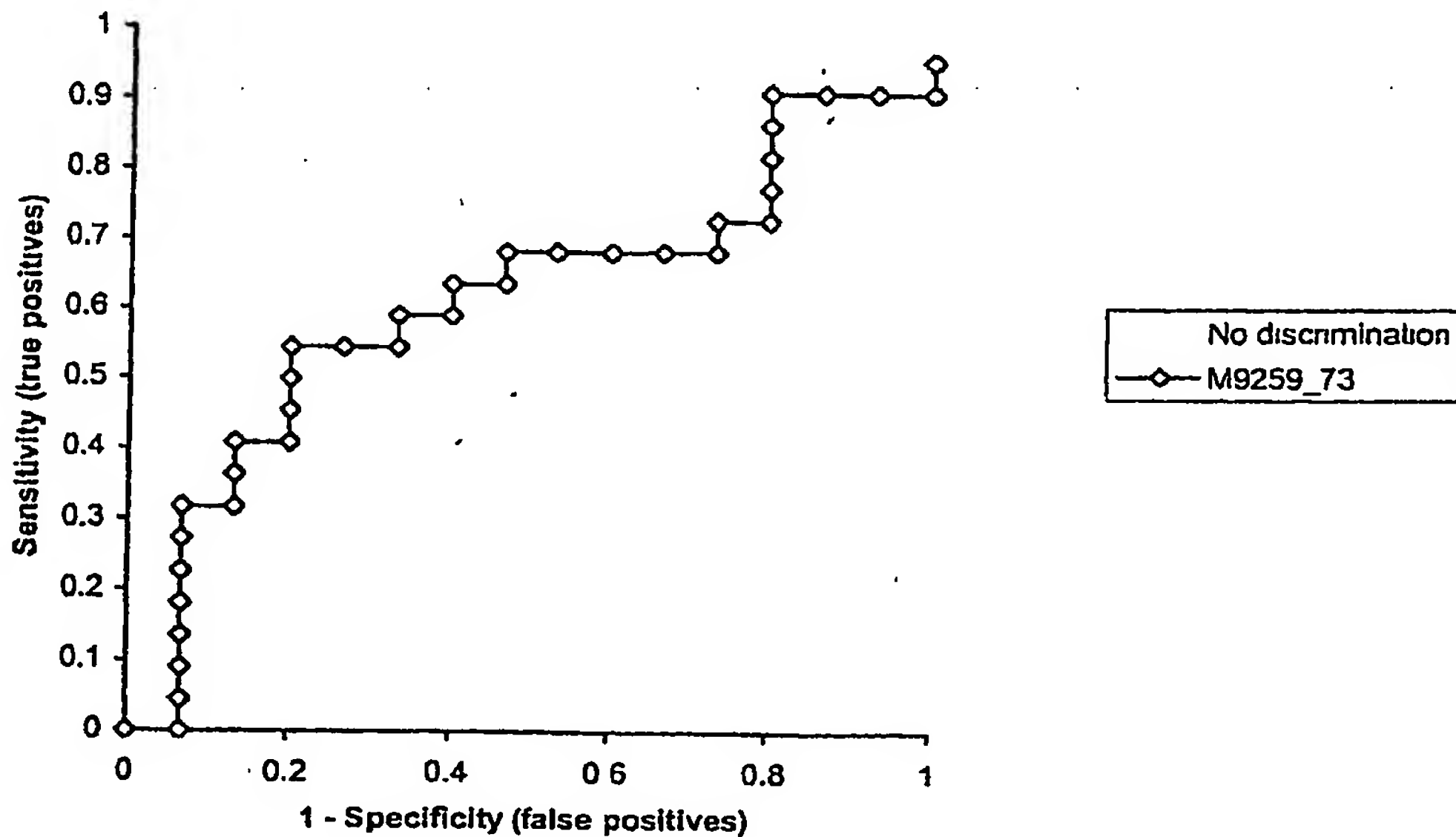
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|-------------------|
| M9259_73 | 0.615 | 0.0949 | 0.1124 | 0.429 to 0.801 | have lower values |



| M9259_73
(abnormals below cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| -0.313072149 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

Test Receiver Operator Characteristic (ROC) curves

M9259_73 by SAMP_GRP

| Performed by | Date | | | | | |
|--------------|-------|-------|----|----|----|----|
| -0.090034929 | 0.0% | 93.3% | 0 | 14 | 1 | 22 |
| -0.087657336 | 4.5% | 93.3% | 1 | 14 | 1 | 21 |
| 0.025059587 | 9.1% | 93.3% | 2 | 14 | 1 | 20 |
| 0.0890659 | 13.6% | 93.3% | 3 | 14 | 1 | 19 |
| 0.137712694 | 18.2% | 93.3% | 4 | 14 | 1 | 18 |
| 0.39484115 | 22.7% | 93.3% | 5 | 14 | 1 | 17 |
| 0.441429925 | 27.3% | 93.3% | 6 | 14 | 1 | 16 |
| 0.443883635 | 31.8% | 93.3% | 7 | 14 | 1 | 15 |
| 0.537223872 | 31.8% | 86.7% | 7 | 13 | 2 | 15 |
| 0.573660892 | 36.4% | 86.7% | 8 | 13 | 2 | 14 |
| 0.587299677 | 40.9% | 86.7% | 9 | 13 | 2 | 13 |
| 1.141788822 | 40.9% | 80.0% | 9 | 12 | 3 | 13 |
| 1.288678045 | 45.5% | 80.0% | 10 | 12 | 3 | 12 |
| 1.497411002 | 50.0% | 80.0% | 11 | 12 | 3 | 11 |
| 1.504448557 | 54.5% | 80.0% | 12 | 12 | 3 | 10 |
| 1.553203734 | 54.5% | 73.3% | 12 | 11 | 4 | 10 |
| 1.697719129 | 54.5% | 66.7% | 12 | 10 | 5 | 10 |
| 1.740725515 | 59.1% | 66.7% | 13 | 10 | 5 | 9 |
| 1.789909879 | 59.1% | 60.0% | 13 | 9 | 6 | 9 |
| 1.800103417 | 63.6% | 60.0% | 14 | 9 | 6 | 8 |
| 1.890731101 | 63.6% | 53.3% | 14 | 8 | 7 | 8 |
| 2.089011337 | 68.2% | 53.3% | 15 | 8 | 7 | 7 |
| 2.450853521 | 68.2% | 46.7% | 15 | 7 | 8 | 7 |
| 3.183220714 | 68.2% | 40.0% | 15 | 6 | 9 | 7 |
| 3.601972595 | 68.2% | 33.3% | 15 | 5 | 10 | 7 |
| 4.117866168 | 68.2% | 26.7% | 15 | 4 | 11 | 7 |
| 4.834268435 | 72.7% | 26.7% | 16 | 4 | 11 | 6 |
| 5.638919739 | 72.7% | 20.0% | 16 | 3 | 12 | 6 |
| 6.10658428 | 77.3% | 20.0% | 17 | 3 | 12 | 5 |
| 6.841923307 | 81.8% | 20.0% | 18 | 3 | 12 | 4 |
| 8.231907094 | 86.4% | 20.0% | 19 | 3 | 12 | 3 |
| 10.42225494 | 90.9% | 20.0% | 20 | 3 | 12 | 2 |
| 15.5536609 | 90.9% | 13.3% | 20 | 2 | 13 | 2 |
| 16.22326061 | 90.9% | 6.7% | 20 | 1 | 14 | 2 |
| 53.13230616 | 90.9% | 0.0% | 20 | 0 | 15 | 2 |
| 69.60587743 | 95.5% | 0.0% | 21 | 0 | 15 | 1 |

916 WID

analysed with Analyse-it - Clinical Laboratory 1 62

Test Receiver Operator Characteristic (ROC) curves

M9612_27 by SAMP_GRP

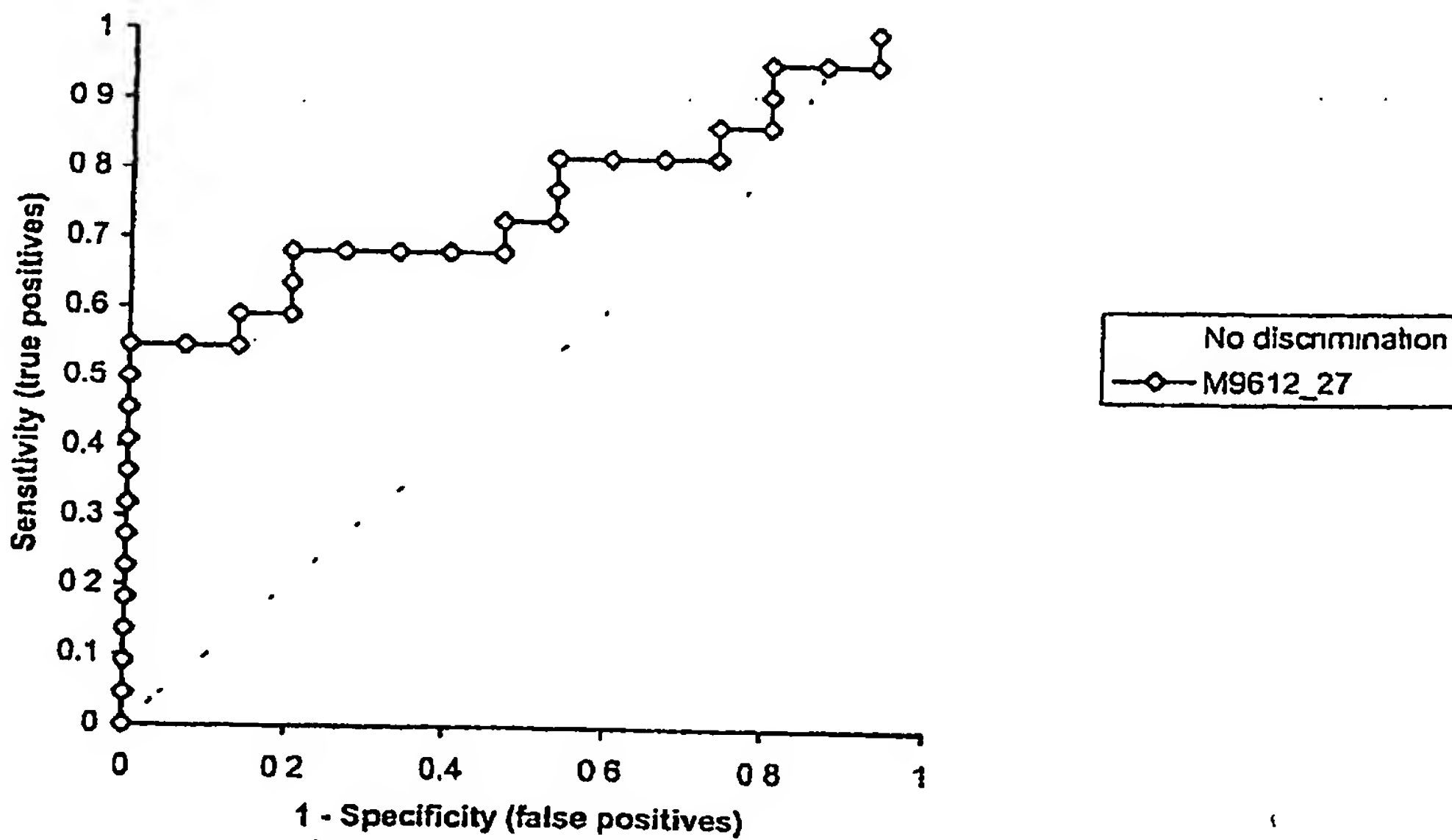
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|-------------------|
| M9612_27 | 0.758 | 0.0789 | 0.0005 | 0.603 to 0.912 | have lower values |



| M9612_27
(abnormals below cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| -0.242818201 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

Test Receiver Operator Characteristic (ROC) curves

M9612_27 by SAMP_GRP

| Performed by | | | | | Date | |
|--------------|--------|--------|----|----|------|----|
| 0.758601683 | 4.5% | 100.0% | 1 | 15 | 0 | 21 |
| 1.180865799 | 9.1% | 100.0% | 2 | 15 | 0 | 20 |
| 1.274578224 | 13.6% | 100.0% | 3 | 15 | 0 | 19 |
| 1.483956338 | 18.2% | 100.0% | 4 | 15 | 0 | 18 |
| 1.493244123 | 22.7% | 100.0% | 5 | 15 | 0 | 17 |
| 1.555852667 | 27.3% | 100.0% | 6 | 15 | 0 | 16 |
| 2.105803209 | 31.8% | 100.0% | 7 | 15 | 0 | 15 |
| 2.369291433 | 36.4% | 100.0% | 8 | 15 | 0 | 14 |
| 2.40902558 | 40.9% | 100.0% | 9 | 15 | 0 | 13 |
| 2.861582232 | 45.5% | 100.0% | 10 | 15 | 0 | 12 |
| 3.208838829 | 50.0% | 100.0% | 11 | 15 | 0 | 11 |
| 4.314256863 | 54.5% | 100.0% | 12 | 15 | 0 | 10 |
| 5.123782783 | 54.5% | 93.3% | 12 | 14 | 1 | 10 |
| 5.206522974 | 54.5% | 86.7% | 12 | 13 | 2 | 10 |
| 5.392504287 | 59.1% | 86.7% | 13 | 13 | 2 | 9 |
| 5.627164435 | 59.1% | 80.0% | 13 | 12 | 3 | 9 |
| 7.347091898 | 63.6% | 80.0% | 14 | 12 | 3 | 8 |
| 7.614016057 | 68.2% | 80.0% | 15 | 12 | 3 | 7 |
| 7.780212345 | 68.2% | 73.3% | 15 | 11 | 4 | 7 |
| 8.066501227 | 68.2% | 66.7% | 15 | 10 | 5 | 7 |
| 8.189857251 | 68.2% | 60.0% | 15 | 9 | 6 | 7 |
| 8.879133228 | 68.2% | 53.3% | 15 | 8 | 7 | 7 |
| 9.452288319 | 72.7% | 53.3% | 16 | 8 | 7 | 6 |
| 10.02350022 | 72.7% | 46.7% | 16 | 7 | 8 | 6 |
| 11.09534531 | 77.3% | 46.7% | 17 | 7 | 8 | 5 |
| 13.60423119 | 81.8% | 46.7% | 18 | 7 | 8 | 4 |
| 13.97510631 | 81.8% | 40.0% | 18 | 6 | 9 | 4 |
| 14.24114764 | 81.8% | 33.3% | 18 | 5 | 10 | 4 |
| 14.30357042 | 81.8% | 26.7% | 18 | 4 | 11 | 4 |
| 14.66718773 | 86.4% | 26.7% | 19 | 4 | 11 | 3 |
| 16.79245222 | 86.4% | 20.0% | 19 | 3 | 12 | 3 |
| 17.49682083 | 90.9% | 20.0% | 20 | 3 | 12 | 2 |
| 32.76755785 | 95.5% | 20.0% | 21 | 3 | 12 | 1 |
| 35.34829908 | 95.5% | 13.3% | 21 | 2 | 13 | 1 |
| 49.72699286 | 95.5% | 6.7% | 21 | 1 | 14 | 1 |
| 74.09042786 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

Test | Receiver Operator Characteristic (ROC) curves

M9746_54 by SAMP_GRP

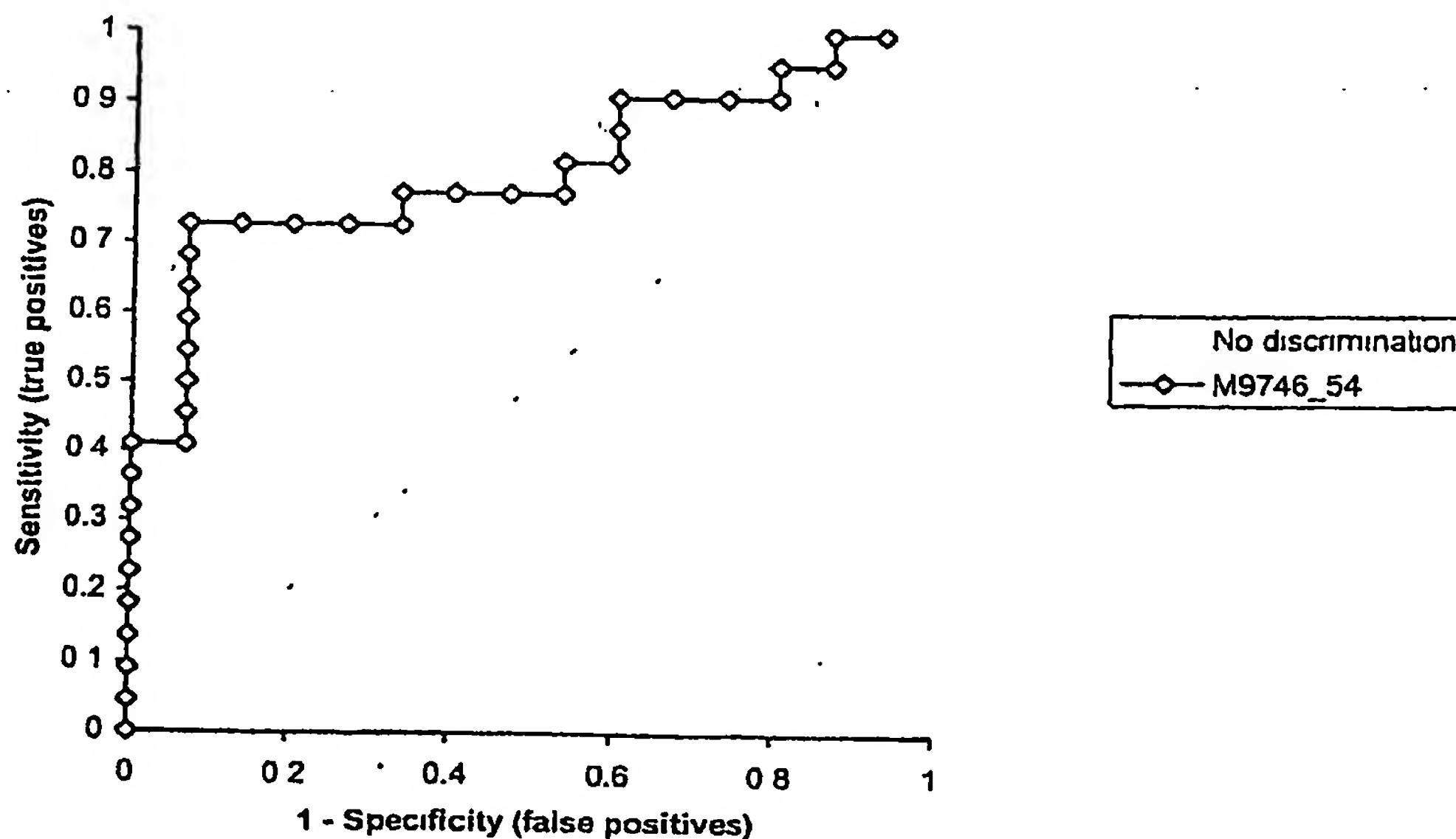
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|---------|----------------|-------------------|
| M9746_54 | 0.809 | 0.0718 | <0.0001 | 0.668 to 0.950 | have lower values |



| M9746_54
(abnormals below cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 0.27462008 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

| Test | | Receiver Operator Characteristic (ROC) curves | | | | | | analysed with Analyse-ii + Clinical Laboratory 1 | |
|--------------|--------|---|----|----|----|----|--|--|--|
| | | M9746_54 by SAMP_GRP | | | | | | | |
| Performed by | | | | | | | | Date | |
| 0.944941397 | 4.5% | 100.0% | 1 | 15 | 0 | 21 | | | |
| 1.429602659 | 9.1% | 100.0% | 2 | 15 | 0 | 20 | | | |
| 1.860367717 | 13.6% | 100.0% | 3 | 15 | 0 | 19 | | | |
| 2.156058253 | 18.2% | 100.0% | 4 | 15 | 0 | 18 | | | |
| 2.163995771 | 22.7% | 100.0% | 5 | 15 | 0 | 17 | | | |
| 2.230258934 | 27.3% | 100.0% | 6 | 15 | 0 | 16 | | | |
| 2.244471438 | 31.8% | 100.0% | 7 | 15 | 0 | 15 | | | |
| 3.928575765 | 36.4% | 100.0% | 8 | 15 | 0 | 14 | | | |
| 4.89314159 | 40.9% | 100.0% | 9 | 15 | 0 | 13 | | | |
| 5.001978398 | 40.9% | 93.3% | 9 | 14 | 1 | 13 | | | |
| 5.395387778 | 45.5% | 93.3% | 10 | 14 | 1 | 12 | | | |
| 5.591140256 | 50.0% | 93.3% | 11 | 14 | 1 | 11 | | | |
| 5.705310247 | 54.5% | 93.3% | 12 | 14 | 1 | 10 | | | |
| 6.346787733 | 59.1% | 93.3% | 13 | 14 | 1 | 9 | | | |
| 6.900258793 | 63.6% | 93.3% | 14 | 14 | 1 | 8 | | | |
| 9.925793863 | 68.2% | 93.3% | 15 | 14 | 1 | 7 | | | |
| 10.99991811 | 72.7% | 93.3% | 16 | 14 | 1 | 6 | | | |
| 12.12215213 | 72.7% | 86.7% | 16 | 13 | 2 | 6 | | | |
| 12.15934553 | 72.7% | 80.0% | 16 | 12 | 3 | 6 | | | |
| 12.53847818 | 72.7% | 73.3% | 16 | 11 | 4 | 6 | | | |
| 12.7064395 | 72.7% | 66.7% | 16 | 10 | 5 | 6 | | | |
| 13.41035628 | 77.3% | 66.7% | 17 | 10 | 5 | 5 | | | |
| 13.44152165 | 77.3% | 60.0% | 17 | 9 | 6 | 5 | | | |
| 13.65324412 | 77.3% | 53.3% | 17 | 8 | 7 | 5 | | | |
| 14.17991663 | 77.3% | 46.7% | 17 | 7 | 8 | 5 | | | |
| 15.57075291 | 81.8% | 46.7% | 18 | 7 | 8 | 4 | | | |
| 18.04349193 | 81.8% | 40.0% | 18 | 6 | 9 | 4 | | | |
| 22.3977826 | 86.4% | 40.0% | 19 | 6 | 9 | 3 | | | |
| 23.32377482 | 90.9% | 40.0% | 20 | 6 | 9 | 2 | | | |
| 24.62590135 | 90.9% | 33.3% | 20 | 5 | 10 | 2 | | | |
| 24.70430526 | 90.9% | 26.7% | 20 | 4 | 11 | 2 | | | |
| 27.58682672 | 90.9% | 20.0% | 20 | 3 | 12 | 2 | | | |
| 31.43474846 | 95.5% | 20.0% | 21 | 3 | 12 | 1 | | | |
| 33.81750113 | 95.5% | 13.3% | 21 | 2 | 13 | 1 | | | |
| 40.01851039 | 100.0% | 13.3% | 22 | 2 | 13 | 0 | | | |
| 54.47066069 | 100.0% | 6.7% | 22 | 1 | 14 | 0 | | | |

9/8 KD

Test Receiver Operator Characteristic (ROC) curves

M9782_13 by SAMP_GRP

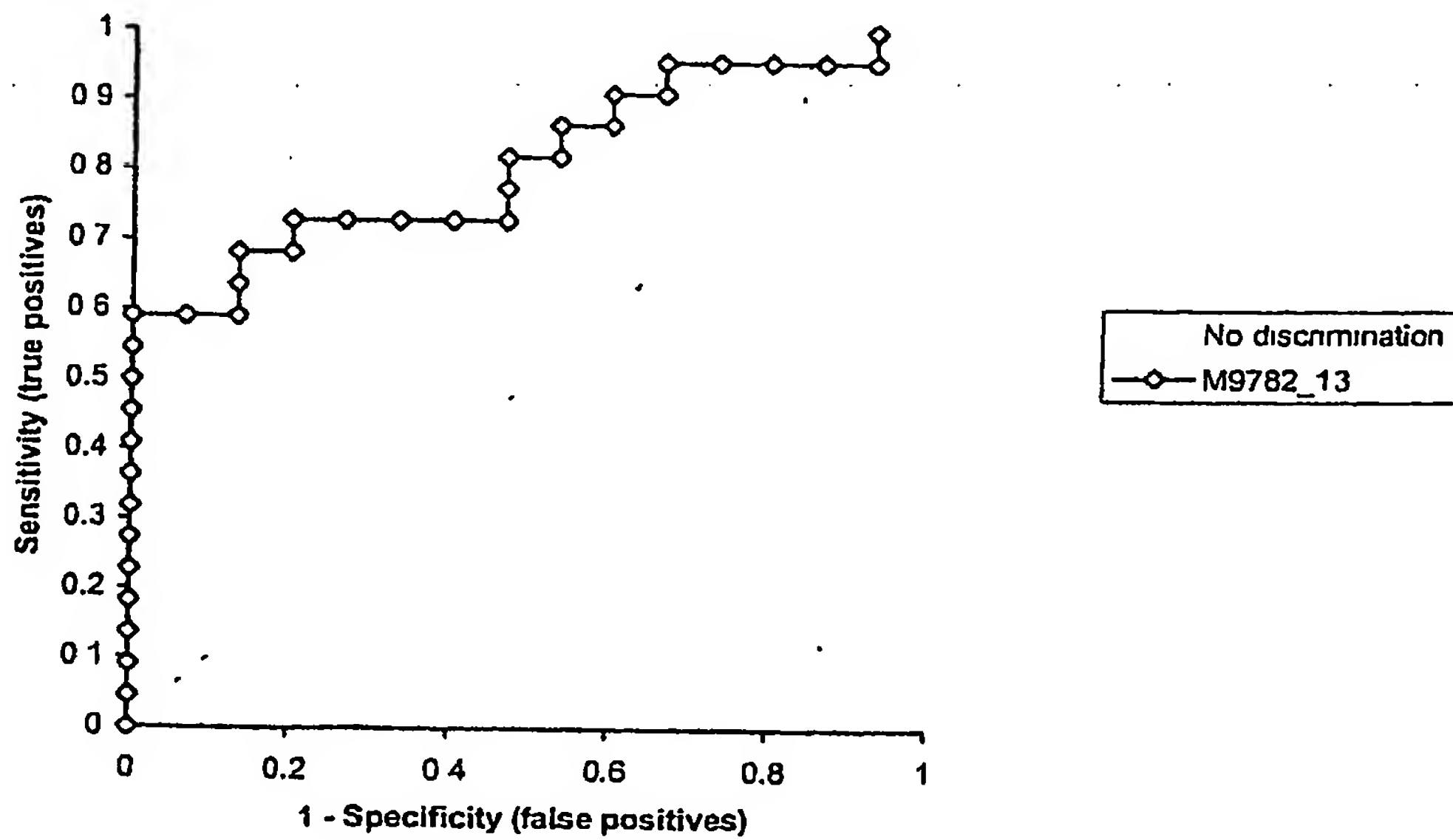
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|---------|----------------|-------------------|
| M9782_13 | 0.812 | 0.0699 | <0.0001 | 0.675 to 0.949 | have lower values |



| M9782_13
(abnormals below cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 0.187949677 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

Test Receiver Operator Characteristic (ROC) curves

M9782_13 by SAMP_GRP

| Performed by | | | | | Date | |
|--------------|--------|--------|----|----|------|----|
| 0.311940904 | 4.5% | 100.0% | 1 | 15 | 0 | 21 |
| 0.320787249 | 9.1% | 100.0% | 2 | 15 | 0 | 20 |
| 0.588458192 | 13.6% | 100.0% | 3 | 15 | 0 | 19 |
| 0.827319355 | 18.2% | 100.0% | 4 | 15 | 0 | 18 |
| 0.964527145 | 22.7% | 100.0% | 5 | 15 | 0 | 17 |
| 1.303108694 | 27.3% | 100.0% | 6 | 15 | 0 | 16 |
| 1.440991138 | 31.8% | 100.0% | 7 | 15 | 0 | 15 |
| 1.911425052 | 36.4% | 100.0% | 8 | 15 | 0 | 14 |
| 1.977973759 | 40.9% | 100.0% | 9 | 15 | 0 | 13 |
| 2.704541978 | 45.5% | 100.0% | 10 | 15 | 0 | 12 |
| 3.18696848 | 50.0% | 100.0% | 11 | 15 | 0 | 11 |
| 3.264391167 | 54.5% | 100.0% | 12 | 15 | 0 | 10 |
| 3.649763174 | 59.1% | 100.0% | 13 | 15 | 0 | 9 |
| 4.050829647 | 59.1% | 93.3% | 13 | 14 | 1 | 9 |
| 4.367868931 | 59.1% | 86.7% | 13 | 13 | 2 | 9 |
| 5.033974153 | 63.6% | 86.7% | 14 | 13 | 2 | 8 |
| 5.632684713 | 68.2% | 86.7% | 15 | 13 | 2 | 7 |
| 5.735939585 | 68.2% | 80.0% | 15 | 12 | 3 | 7 |
| 6.576947242 | 72.7% | 80.0% | 16 | 12 | 3 | 6 |
| 6.700781868 | 72.7% | 73.3% | 16 | 11 | 4 | 6 |
| 6.825206697 | 72.7% | 66.7% | 16 | 10 | 5 | 6 |
| 8.182420851 | 72.7% | 60.0% | 16 | 9 | 6 | 6 |
| 8.312179556 | 72.7% | 53.3% | 16 | 8 | 7 | 6 |
| 8.461231786 | 77.3% | 53.3% | 17 | 8 | 7 | 5 |
| 8.604240794 | 81.8% | 53.3% | 18 | 8 | 7 | 4 |
| 10.6034531 | 81.8% | 46.7% | 18 | 7 | 8 | 4 |
| 11.69847523 | 86.4% | 46.7% | 19 | 7 | 8 | 3 |
| 12.95334106 | 86.4% | 40.0% | 19 | 6 | 9 | 3 |
| 14.37960511 | 90.9% | 40.0% | 20 | 6 | 9 | 2 |
| 14.55501121 | 90.9% | 33.3% | 20 | 5 | 10 | 2 |
| 22.8775234 | 95.5% | 33.3% | 21 | 5 | 10 | 1 |
| 24.59587908 | 95.5% | 26.7% | 21 | 4 | 11 | 1 |
| 32.89066637 | 95.5% | 20.0% | 21 | 3 | 12 | 1 |
| 44.04188758 | 95.5% | 13.3% | 21 | 2 | 13 | 1 |
| 47.67700209 | 95.5% | 6.7% | 21 | 1 | 14 | 1 |
| 65.79597195 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

10.0 LD

analysed with Analyse-It + Clinical Laboratory 11

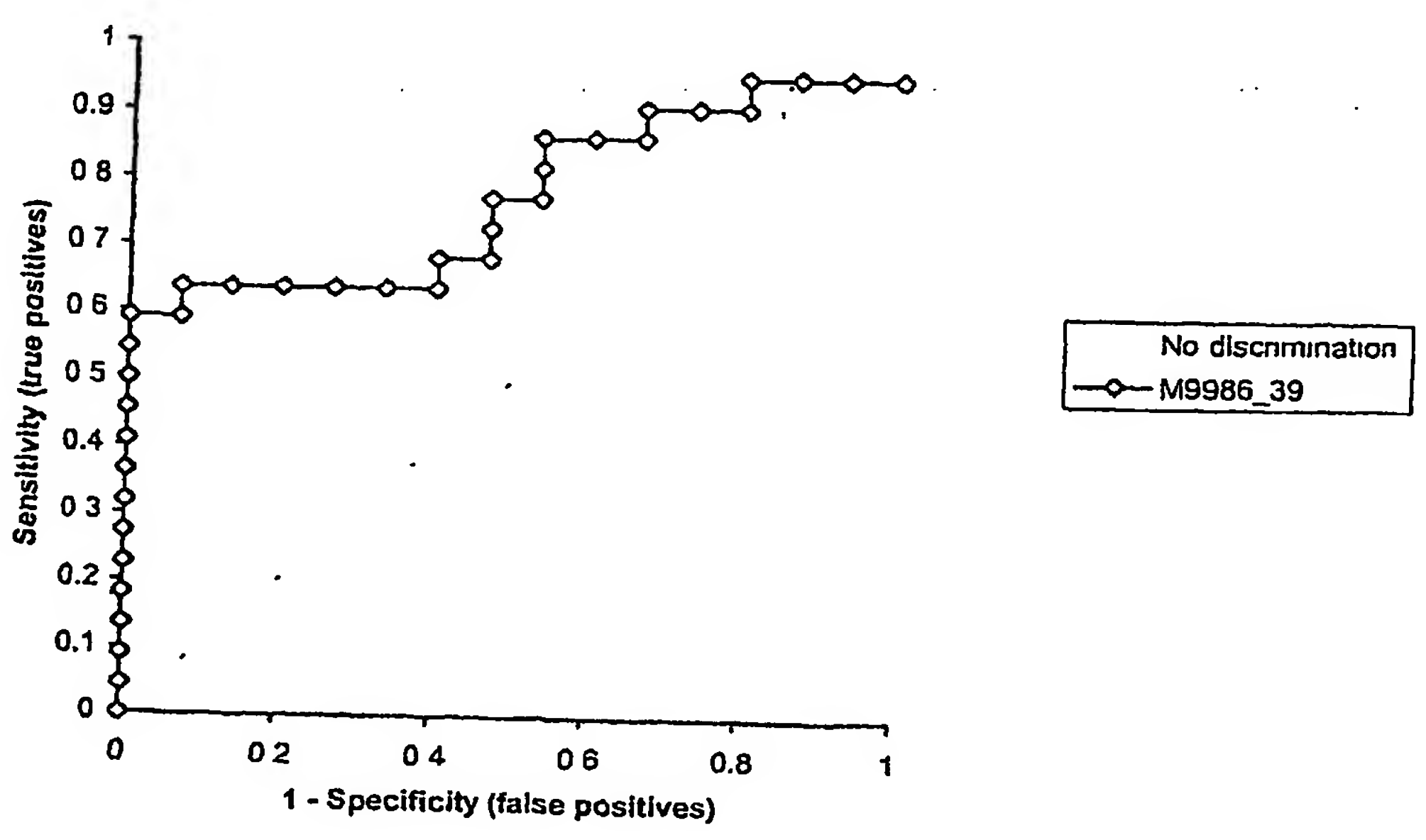
Test Receiver Operator Characteristic (ROC) curves
 M9986_39 by SAMP_GRP

Performed by _____ Date _____

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|-------------------|
| M9986_39 | 0.776 | 0.0767 | 0.0002 | 0.625 to 0.926 | have lower values |



| M9986_39
(abnormals below cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| -0.295256429 | 0.00% | 100.0% | 0 | 15 | 0 | 22 |

Test Receiver Operator Characteristic (ROC) curves

M9986_39 by SAMP_GRP

| Performed by | | | | | | Date | |
|--------------|-------|--------|----|----|----|------|--|
| 1.008835146 | 4.5% | 100.0% | 1 | 15 | 0 | 21 | |
| 1.165659121 | 9.1% | 100.0% | 2 | 15 | 0 | 20 | |
| 1.256851909 | 13.6% | 100.0% | 3 | 15 | 0 | 19 | |
| 2.241283084 | 18.2% | 100.0% | 4 | 15 | 0 | 18 | |
| 2.28786077 | 22.7% | 100.0% | 5 | 15 | 0 | 17 | |
| 2.567899944 | 27.3% | 100.0% | 6 | 15 | 0 | 16 | |
| 2.915542456 | 31.8% | 100.0% | 7 | 15 | 0 | 15 | |
| 2.946087861 | 36.4% | 100.0% | 8 | 15 | 0 | 14 | |
| 3.515636808 | 40.9% | 100.0% | 9 | 15 | 0 | 13 | |
| 3.61887364 | 45.5% | 100.0% | 10 | 15 | 0 | 12 | |
| 4.081298473 | 50.0% | 100.0% | 11 | 15 | 0 | 11 | |
| 4.589735775 | 54.5% | 100.0% | 12 | 15 | 0 | 10 | |
| 5.266312315 | 59.1% | 100.0% | 13 | 15 | 0 | 9 | |
| 7.217859829 | 59.1% | 93.3% | 13 | 14 | 1 | 9 | |
| 8.318176705 | 63.6% | 93.3% | 14 | 14 | 1 | 8 | |
| 8.878907369 | 63.6% | 86.7% | 14 | 13 | 2 | 8 | |
| 9.456901691 | 63.6% | 80.0% | 14 | 12 | 3 | 8 | |
| 10.28999424 | 63.6% | 73.3% | 14 | 11 | 4 | 8 | |
| 14.37846263 | 63.6% | 66.7% | 14 | 10 | 5 | 8 | |
| 16.99313275 | 63.6% | 60.0% | 14 | 9 | 6 | 8 | |
| 18.82439633 | 68.2% | 60.0% | 15 | 9 | 6 | 7 | |
| 19.58359542 | 68.2% | 53.3% | 15 | 8 | 7 | 7 | |
| 20.13834584 | 72.7% | 53.3% | 16 | 8 | 7 | 6 | |
| 22.48639367 | 77.3% | 53.3% | 17 | 8 | 7 | 5 | |
| 23.08411608 | 77.3% | 46.7% | 17 | 7 | 8 | 5 | |
| 25.85315832 | 81.8% | 46.7% | 18 | 7 | 8 | 4 | |
| 29.21510714 | 86.4% | 46.7% | 19 | 7 | 8 | 3 | |
| 30.74984161 | 86.4% | 40.0% | 19 | 6 | 9 | 3 | |
| 32.56932974 | 86.4% | 33.3% | 19 | 5 | 10 | 3 | |
| 37.00175626 | 90.9% | 33.3% | 20 | 5 | 10 | 2 | |
| 40.65070508 | 90.9% | 26.7% | 20 | 4 | 11 | 2 | |
| 46.36510251 | 90.9% | 20.0% | 20 | 3 | 12 | 2 | |
| 59.92837427 | 95.5% | 20.0% | 21 | 3 | 12 | 1 | |
| 60.68808134 | 95.5% | 13.3% | 21 | 2 | 13 | 1 | |
| 97.93584835 | 95.5% | 6.7% | 21 | 1 | 14 | 1 | |
| 104.5984281 | 95.5% | 0.0% | 21 | 0 | 15 | 1 | |

Test | Receiver Operator Characteristic (ROC) curves

M10823_4 by SAMP_GRP

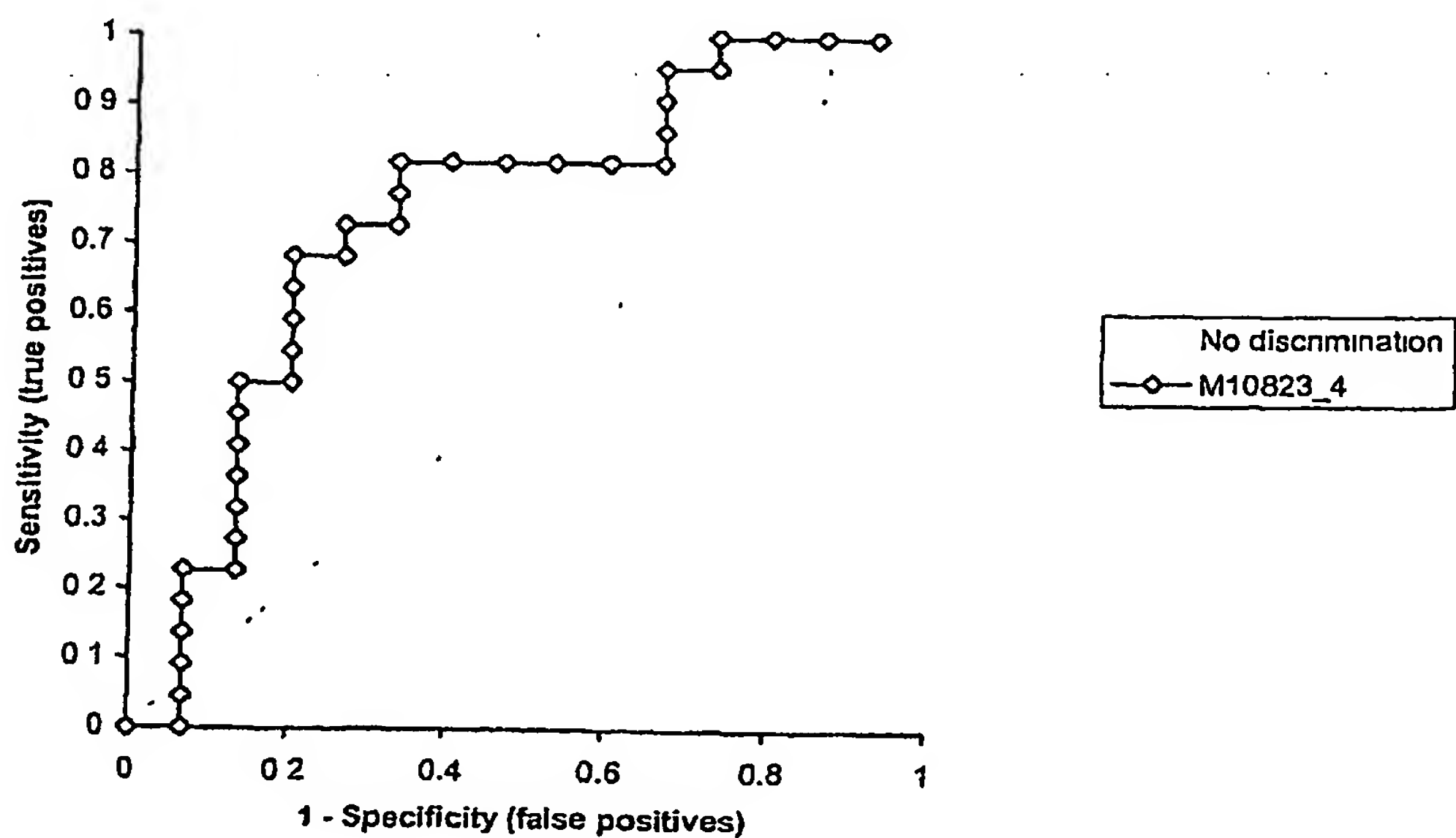
Performed by

Date _____

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M10823_4 | 0.745 | 0.0879 | 0.0026 | 0.573 to 0.918 | have higher values |



| M10823_4
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 0.523085472 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

Test Receiver Operator Characteristic (ROC) curves

M10823_4 by SAMP_GRP

| Performed by | | | | | Date | |
|--------------|--------|--------|----|----|------|----|
| 0.671006585 | 100.0% | 13.3% | 22 | 2 | 13 | 0 |
| 0.673951205 | 100.0% | 20.0% | 22 | 3 | 12 | 0 |
| 0.85034147 | 100.0% | 26.7% | 22 | 4 | 11 | 0 |
| 1.091235144 | 95.5% | 26.7% | 21 | 4 | 11 | 1 |
| 1.499560539 | 95.5% | 33.3% | 21 | 5 | 10 | 1 |
| 1.6038729 | 90.9% | 33.3% | 20 | 5 | 10 | 2 |
| 1.689901778 | 86.4% | 33.3% | 19 | 5 | 10 | 3 |
| 1.873136627 | 81.8% | 33.3% | 18 | 5 | 10 | 4 |
| 1.873452486 | 81.8% | 40.0% | 18 | 6 | 9 | 4 |
| 1.911010945 | 81.8% | 46.7% | 18 | 7 | 8 | 4 |
| 2.024488057 | 81.8% | 53.3% | 18 | 8 | 7 | 4 |
| 2.566194201 | 81.8% | 60.0% | 18 | 9 | 6 | 4 |
| 2.828797509 | 81.8% | 66.7% | 18 | 10 | 5 | 4 |
| 2.900653046 | 77.3% | 66.7% | 17 | 10 | 5 | 5 |
| 2.924282124 | 72.7% | 66.7% | 16 | 10 | 5 | 6 |
| 3.48601262 | 72.7% | 73.3% | 16 | 11 | 4 | 6 |
| 3.508487988 | 68.2% | 73.3% | 15 | 11 | 4 | 7 |
| 4.080371763 | 68.2% | 80.0% | 15 | 12 | 3 | 7 |
| 4.336801503 | 63.6% | 80.0% | 14 | 12 | 3 | 8 |
| 4.685772237 | 59.1% | 80.0% | 13 | 12 | 3 | 9 |
| 5.846072901 | 54.5% | 80.0% | 12 | 12 | 3 | 10 |
| 5.927676181 | 50.0% | 80.0% | 11 | 12 | 3 | 11 |
| 6.051455083 | 50.0% | 86.7% | 11 | 13 | 2 | 11 |
| 6.178395098 | 45.5% | 86.7% | 10 | 13 | 2 | 12 |
| 6.452067205 | 40.9% | 86.7% | 9 | 13 | 2 | 13 |
| 6.802498183 | 36.4% | 86.7% | 8 | 13 | 2 | 14 |
| 8.451155445 | 31.8% | 86.7% | 7 | 13 | 2 | 15 |
| 8.46425216 | 27.3% | 86.7% | 6 | 13 | 2 | 16 |
| 11.36753199 | 22.7% | 86.7% | 5 | 13 | 2 | 17 |
| 15.67369003 | 22.7% | 93.3% | 5 | 14 | 1 | 17 |
| 19.34606204 | 18.2% | 93.3% | 4 | 14 | 1 | 18 |
| 20.10344319 | 13.6% | 93.3% | 3 | 14 | 1 | 19 |
| 20.51485771 | 9.1% | 93.3% | 2 | 14 | 1 | 20 |
| 32.081559 | 4.5% | 93.3% | 1 | 14 | 1 | 21 |
| 44.91333527 | 0.0% | 93.3% | 0 | 14 | 1 | 22 |
| 54.23581573 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

10.9 WD

Test Receiver Operator Characteristic (ROC) curves

M10860_5 by SAMP_GRP

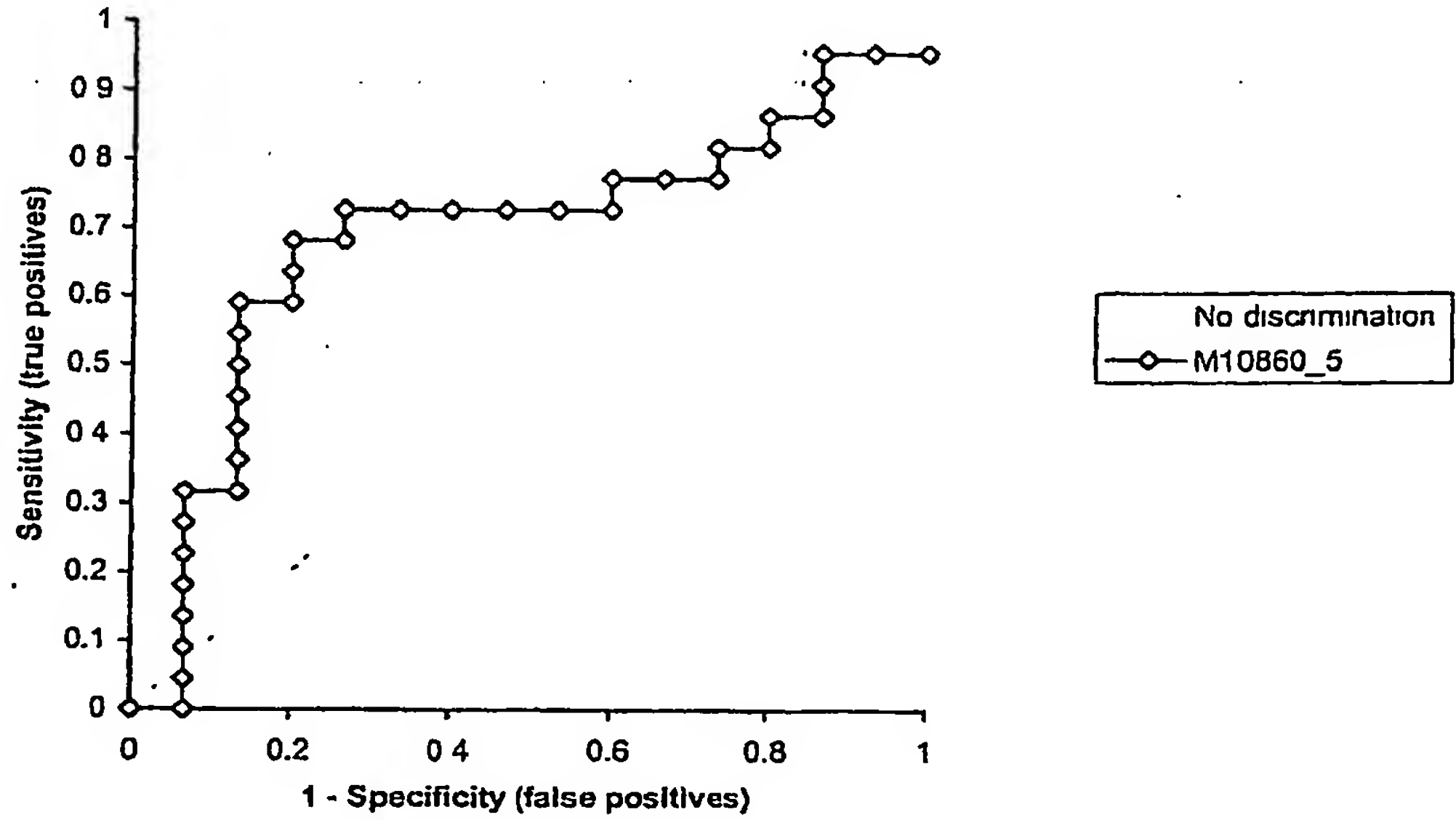
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M10860_5 | 0.691 | 0.0920 | 0.0190 | 0.511 to 0.871 | have higher values |



| M10860_5
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 0.625449592 | 95.5% | 0.0% | 21 | 0 | 15 | 1 |

Test Receiver Operator Characteristic (ROC) curves

M10860_5 by SAMP_GRP

| Performed by | | | | | Date | |
|--------------|-------|--------|----|----|------|----|
| 0.649659093 | 95.5% | 6 7% | 21 | 1 | 14 | 1 |
| 0.75660742 | 95.5% | 13.3% | 21 | 2 | 13 | 1 |
| 0.827850575 | 90.9% | 13.3% | 20 | 2 | 13 | 2 |
| 0.874557025 | 86.4% | 13.3% | 19 | 2 | 13 | 3 |
| 0.942458079 | 86.4% | 20 0% | 19 | 3 | 12 | 3 |
| 1.299508596 | 81.8% | 20.0% | 18 | 3 | 12 | 4 |
| 1.477528139 | 81.8% | 26.7% | 18 | 4 | 11 | 4 |
| 1.741733474 | 77.3% | 26.7% | 17 | 4 | 11 | 5 |
| 2.442650232 | 77.3% | 33 3% | 17 | 5 | 10 | 5 |
| 2.49969861 | 77.3% | 40.0% | 17 | 6 | 9 | 5 |
| 2.854472279 | 72.7% | 40.0% | 16 | 6 | 9 | 6 |
| 3.637781801 | 72.7% | 46 7% | 16 | 7 | 8 | 6 |
| 4.026034745 | 72.7% | 53 3% | 16 | 8 | 7 | 6 |
| 4.373739534 | 72.7% | 60 0% | 16 | 9 | 6 | 6 |
| 4.412232967 | 72.7% | 66.7% | 16 | 10 | 5 | 6 |
| 5.243094923 | 72.7% | 73.3% | 16 | 11 | 4 | 6 |
| 5.879200077 | 68.2% | 73 3% | 15 | 11 | 4 | 7 |
| 7.832574741 | 68.2% | 80 0% | 15 | 12 | 3 | 7 |
| 7.983245257 | 63.6% | 80.0% | 14 | 12 | 3 | 8 |
| 8.502650675 | 59 1% | 80.0% | 13 | 12 | 3 | 9 |
| 9.277844369 | 59.1% | 86.7% | 13 | 13 | 2 | 9 |
| 9.98032986 | 54.5% | 86.7% | 12 | 13 | 2 | 10 |
| 10.446093 | 50.0% | 86.7% | 11 | 13 | 2 | 11 |
| 11.40028173 | 45.5% | 86 7% | 10 | 13 | 2 | 12 |
| 11.96785354 | 40.9% | 86.7% | 9 | 13 | 2 | 13 |
| 13.7323821 | 36.4% | 86.7% | 8 | 13 | 2 | 14 |
| 13.92963359 | 31.8% | 86.7% | 7 | 13 | 2 | 15 |
| 18.38409613 | 31.8% | 93.3% | 7 | 14 | 1 | 15 |
| 21.12109901 | 27 3% | 93.3% | 6 | 14 | 1 | 16 |
| 23.08340021 | 22.7% | 93.3% | 5 | 14 | 1 | 17 |
| 25.98323228 | 18.2% | 93.3% | 4 | 14 | 1 | 18 |
| 28.89121952 | 13.6% | 93.3% | 3 | 14 | 1 | 19 |
| 55.22611991 | 9 1% | 93.3% | 2 | 14 | 1 | 20 |
| 131.6364922 | 4 5% | 93.3% | 1 | 14 | 1 | 21 |
| 194.5375406 | 0.0% | 93.3% | 0 | 14 | 1 | 22 |
| 251.7598007 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

11.13.2013

analysed with Analyse-ii + Clinical Laboratory 1 62

Test Receiver Operator Characteristic (ROC) curves

M11298_6 by SAMP_GRP

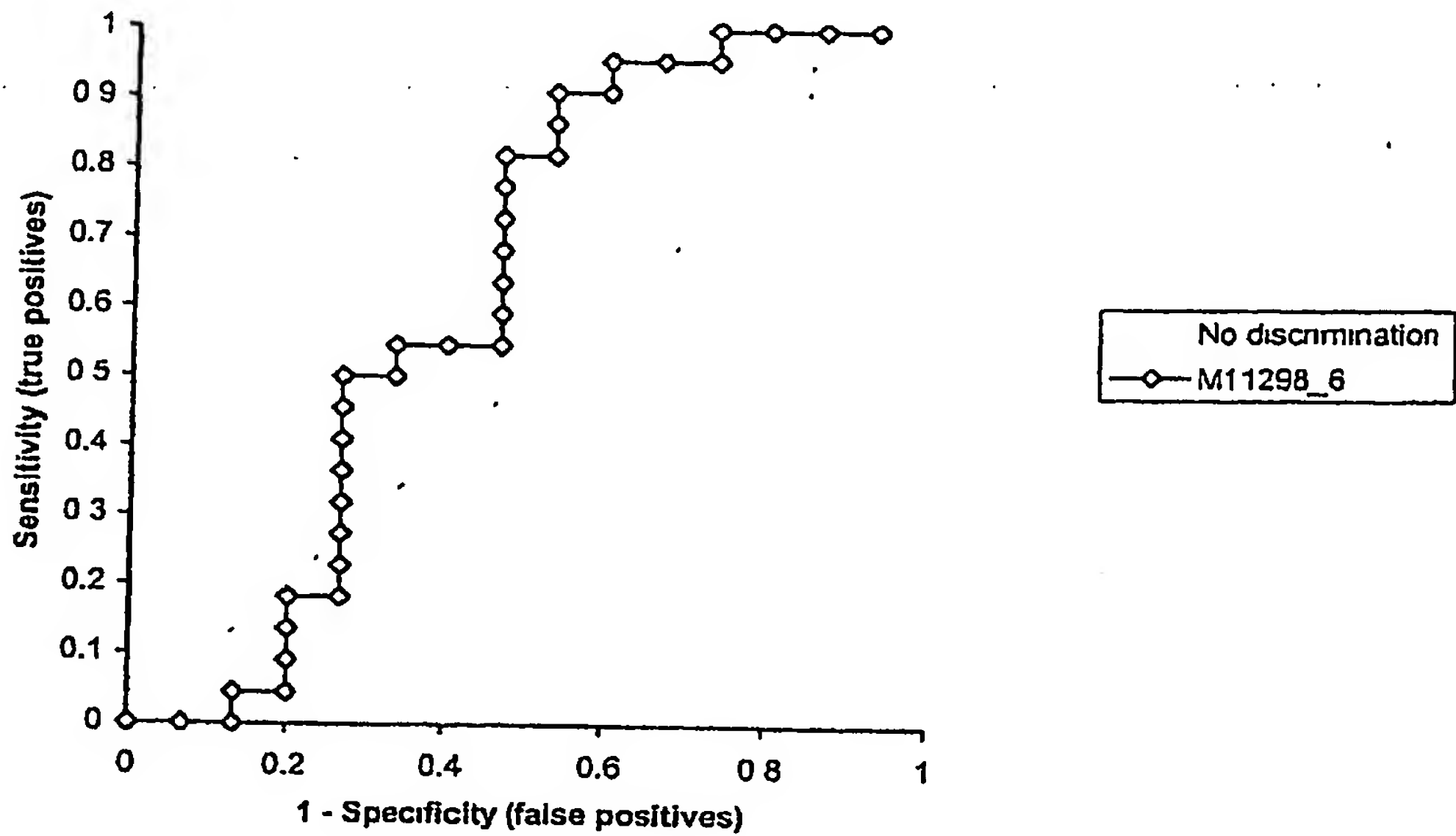
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M11298_6 | 0.630 | 0.1058 | 0.1091 | 0.423 to 0.838 | have higher values |



| M11298_6
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 0.069735482 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

Test Receiver Operator Characteristic (ROC) curves

M11298_6 by SAMP_GRP

| Performed by | Date | | | | | |
|--------------|--------|--------|----|----|----|----|
| 0.149582527 | 100.0% | 13.3% | 22 | 2 | 13 | 0 |
| 0.223497018 | 100.0% | 20.0% | 22 | 3 | 12 | 0 |
| 0.288031269 | 100.0% | 26.7% | 22 | 4 | 11 | 0 |
| 0.392039963 | 95.5% | 26.7% | 21 | 4 | 11 | 1 |
| 0.482206326 | 95.5% | 33.3% | 21 | 5 | 10 | 1 |
| 0.493313078 | 95.5% | 40.0% | 21 | 6 | 9 | 1 |
| 0.567621858 | 90.9% | 40.0% | 20 | 6 | 9 | 2 |
| 0.581373026 | 90.9% | 46.7% | 20 | 7 | 8 | 2 |
| 0.68372028 | 86.4% | 46.7% | 19 | 7 | 8 | 3 |
| 0.705154358 | 81.8% | 46.7% | 18 | 7 | 8 | 4 |
| 1.022125197 | 81.8% | 53.3% | 18 | 8 | 7 | 4 |
| 1.396624672 | 77.3% | 53.3% | 17 | 8 | 7 | 5 |
| 1.626040888 | 72.7% | 53.3% | 16 | 8 | 7 | 6 |
| 1.75309758 | 68.2% | 53.3% | 15 | 8 | 7 | 7 |
| 1.78154363 | 63.6% | 53.3% | 14 | 8 | 7 | 8 |
| 1.907771234 | 59.1% | 53.3% | 13 | 8 | 7 | 9 |
| 1.971133683 | 54.5% | 53.3% | 12 | 8 | 7 | 10 |
| 2.262083652 | 54.5% | 60.0% | 12 | 9 | 6 | 10 |
| 2.529965406 | 54.5% | 66.7% | 12 | 10 | 5 | 10 |
| 2.604054361 | 50.0% | 66.7% | 11 | 10 | 5 | 11 |
| 3.647733064 | 50.0% | 73.3% | 11 | 11 | 4 | 11 |
| 4.380208717 | 45.5% | 73.3% | 10 | 11 | 4 | 12 |
| 6.698383023 | 40.9% | 73.3% | 9 | 11 | 4 | 13 |
| 6.760494031 | 36.4% | 73.3% | 8 | 11 | 4 | 14 |
| 7.443587208 | 31.8% | 73.3% | 7 | 11 | 4 | 15 |
| 8.262329904 | 27.3% | 73.3% | 6 | 11 | 4 | 16 |
| 9.003081752 | 22.7% | 73.3% | 5 | 11 | 4 | 17 |
| 11.5832935 | 18.2% | 73.3% | 4 | 11 | 4 | 18 |
| 11.61282227 | 18.2% | 80.0% | 4 | 12 | 3 | 18 |
| 18.74142022 | 13.6% | 80.0% | 3 | 12 | 3 | 19 |
| 19.38284104 | 9.1% | 80.0% | 2 | 12 | 3 | 20 |
| 24.23295792 | 4.5% | 80.0% | 1 | 12 | 3 | 21 |
| 26.16048385 | 4.5% | 86.7% | 1 | 13 | 2 | 21 |
| 26.36644348 | 0.0% | 86.7% | 0 | 13 | 2 | 22 |
| 32.88581786 | 0.0% | 93.3% | 0 | 14 | 1 | 22 |
| 39.19350134 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

13.4 KD

11.11.2019 11:11:11

analysed with Analyse-It + Clinical Laboratory 16

Test Receiver Operator Characteristic (ROC) curves

M13386_4 by SAMP_GRP

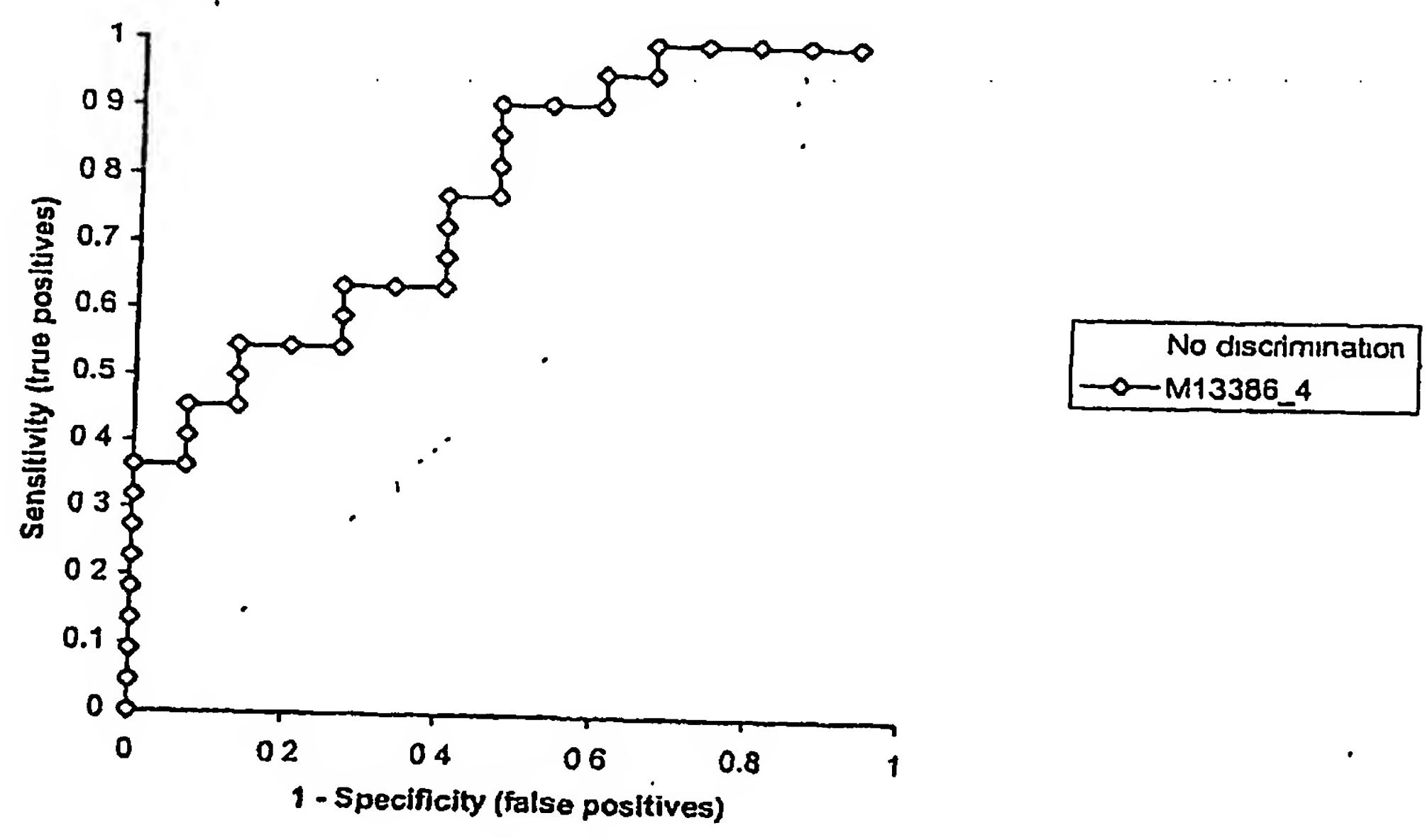
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|---------|----------------|--------------------|
| M13386_4 | 0.782 | 0.0756 | <0.0001 | 0.634 to 0.930 | have higher values |



| M13386_4
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 0.09381789 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

13.9 KD

31.03.2020 14:00:00

analysed with Analyse-it - Clinical Laboratory

Test Receiver Operator Characteristic (ROC) curves

M13893_9 by SAMP_GRP

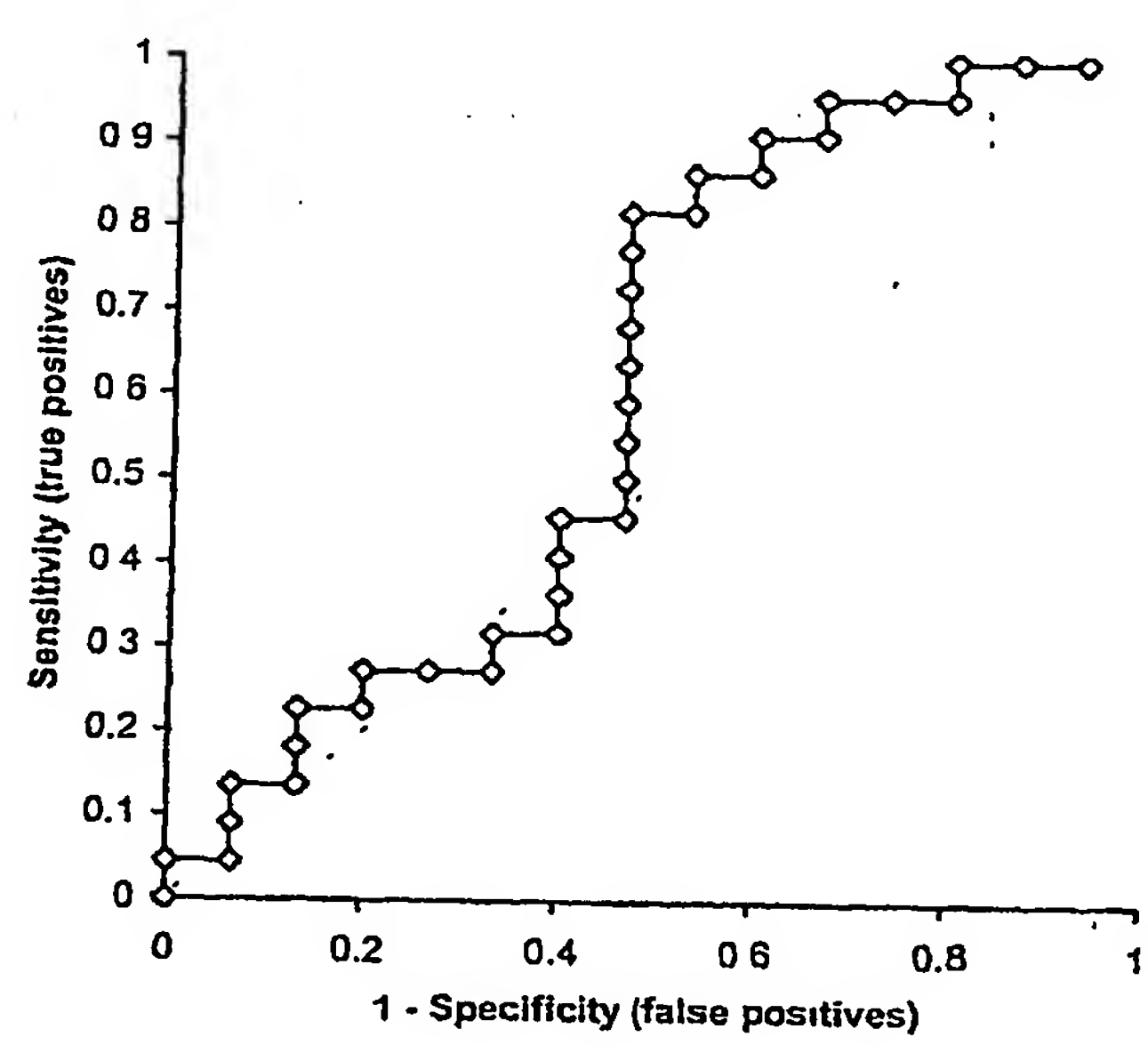
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M13893_9 | 0.615 | 0.1028 | 0.1313 | 0.414 to 0.817 | have higher values |



| M13893_9
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 0.628842989 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

Test Receiver Operator Characteristic (ROC) curves

M13893_9 by SAMP_GRP

| Performed by | Date | | | | | |
|--------------|--------|--------|----|----|----|----|
| 0.743225364 | 100.0% | 13.3% | 22 | 2 | 13 | 0 |
| 1.030426576 | 100.0% | 20.0% | 22 | 3 | 12 | 0 |
| 1.380127971 | 95.5% | 20.0% | 21 | 3 | 12 | 1 |
| 1.426474539 | 95.5% | 26.7% | 21 | 4 | 11 | 1 |
| 2.152972601 | 95.5% | 33.3% | 21 | 5 | 10 | 1 |
| 2.608056213 | 90.9% | 33.3% | 20 | 5 | 10 | 2 |
| 2.630865033 | 90.9% | 40.0% | 20 | 6 | 9 | 2 |
| 2.659269738 | 86.4% | 40.0% | 19 | 6 | 9 | 3 |
| 3.259037701 | 86.4% | 46.7% | 19 | 7 | 8 | 3 |
| 3.270230475 | 81.8% | 46.7% | 18 | 7 | 8 | 4 |
| 3.291970055 | 81.8% | 53.3% | 18 | 8 | 7 | 4 |
| 3.900053221 | 77.3% | 53.3% | 17 | 8 | 7 | 5 |
| 4.191044639 | 72.7% | 53.3% | 16 | 8 | 7 | 6 |
| 6.145344315 | 68.2% | 53.3% | 15 | 8 | 7 | 7 |
| 6.644038085 | 63.6% | 53.3% | 14 | 8 | 7 | 8 |
| 8.02492889 | 59.1% | 53.3% | 13 | 8 | 7 | 9 |
| 8.320312383 | 54.5% | 53.3% | 12 | 8 | 7 | 10 |
| 8.499048941 | 50.0% | 53.3% | 11 | 8 | 7 | 11 |
| 8.831927477 | 45.5% | 53.3% | 10 | 8 | 7 | 12 |
| 9.856140439 | 45.5% | 60.0% | 10 | 9 | 6 | 12 |
| 10.62746905 | 40.9% | 60.0% | 9 | 9 | 6 | 13 |
| 10.82610414 | 36.4% | 60.0% | 8 | 9 | 6 | 14 |
| 12.54454288 | 31.8% | 60.0% | 7 | 9 | 6 | 15 |
| 13.90470058 | 31.8% | 66.7% | 7 | 10 | 5 | 15 |
| 14.27519579 | 27.3% | 66.7% | 6 | 10 | 5 | 16 |
| 14.81217871 | 27.3% | 73.3% | 6 | 11 | 4 | 16 |
| 15.05367835 | 27.3% | 80.0% | 6 | 12 | 3 | 16 |
| 15.93348534 | 22.7% | 80.0% | 5 | 12 | 3 | 17 |
| 17.30998863 | 22.7% | 86.7% | 5 | 13 | 2 | 17 |
| 21.0557198 | 18.2% | 86.7% | 4 | 13 | 2 | 18 |
| 21.90739293 | 13.6% | 86.7% | 3 | 13 | 2 | 19 |
| 22.91996482 | 13.6% | 93.3% | 3 | 14 | 1 | 19 |
| 27.95243119 | 9.1% | 93.3% | 2 | 14 | 1 | 20 |
| 29.69045585 | 4.5% | 93.3% | 1 | 14 | 1 | 21 |
| 36.34488613 | 4.5% | 100.0% | 1 | 15 | 0 | 21 |
| 127.7527799 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

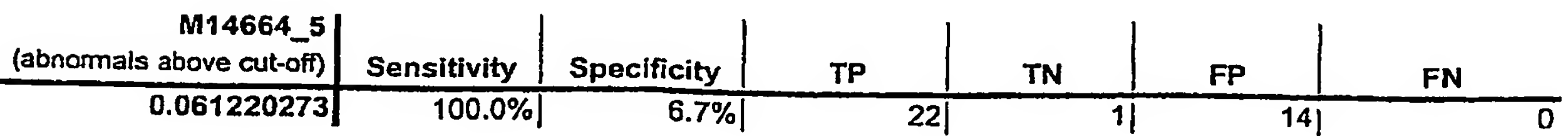
Test | Receiver Operator Characteristic (ROC) curves

Performed by

Date

n | 37

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M14664_5 | 0.612 | 0.0959 | 0.1211 | 0.424 to 0.800 | have higher values |



Test Receiver Operator Characteristic (ROC) curves

M14664_5 by SAMP_GRP

| Performed by | | | | | Date | |
|--------------|-------|--------|----|----|------|----|
| 0.141560818 | 95.5% | 6.7% | 21 | 1 | 14 | 1 |
| 0.420364231 | 90.9% | 6.7% | 20 | 1 | 14 | 2 |
| 0.460694086 | 86.4% | 6.7% | 19 | 1 | 14 | 3 |
| 0.651725392 | 81.8% | 6.7% | 18 | 1 | 14 | 4 |
| 0.669942947 | 81.8% | 13.3% | 18 | 2 | 13 | 4 |
| 0.676613432 | 81.8% | 20.0% | 18 | 3 | 12 | 4 |
| 0.716768642 | 77.3% | 20.0% | 17 | 3 | 12 | 5 |
| 0.831765072 | 77.3% | 26.7% | 17 | 4 | 11 | 5 |
| 0.86823056 | 77.3% | 33.3% | 17 | 5 | 10 | 5 |
| 0.8845323 | 77.3% | 40.0% | 17 | 6 | 9 | 5 |
| 1.170116981 | 77.3% | 46.7% | 17 | 7 | 8 | 5 |
| 1.213470147 | 77.3% | 53.3% | 17 | 8 | 7 | 5 |
| 1.220792267 | 72.7% | 53.3% | 16 | 8 | 7 | 6 |
| 1.237617785 | 72.7% | 60.0% | 16 | 9 | 6 | 6 |
| 1.348864013 | 68.2% | 60.0% | 15 | 9 | 6 | 7 |
| 1.48726478 | 63.6% | 60.0% | 14 | 9 | 6 | 8 |
| 1.531760922 | 59.1% | 60.0% | 13 | 9 | 6 | 9 |
| 1.586845037 | 59.1% | 66.7% | 13 | 10 | 5 | 9 |
| 1.666566621 | 54.5% | 66.7% | 12 | 10 | 5 | 10 |
| 1.724981193 | 50.0% | 66.7% | 11 | 10 | 5 | 11 |
| 3.302147733 | 45.5% | 66.7% | 10 | 10 | 5 | 12 |
| 3.486304719 | 45.5% | 73.3% | 10 | 11 | 4 | 12 |
| 3.551218748 | 40.9% | 73.3% | 9 | 11 | 4 | 13 |
| 3.916000499 | 36.4% | 73.3% | 8 | 11 | 4 | 14 |
| 4.994468705 | 36.4% | 80.0% | 8 | 12 | 3 | 14 |
| 7.660385297 | 31.8% | 80.0% | 7 | 12 | 3 | 15 |
| 8.303404038 | 27.3% | 80.0% | 6 | 12 | 3 | 16 |
| 8.332740901 | 27.3% | 86.7% | 6 | 13 | 2 | 16 |
| 10.53190359 | 22.7% | 86.7% | 5 | 13 | 2 | 17 |
| 11.0878473 | 18.2% | 86.7% | 4 | 13 | 2 | 18 |
| 14.9303935 | 18.2% | 93.3% | 4 | 14 | 1 | 18 |
| 20.5759742 | 13.6% | 93.3% | 3 | 14 | 1 | 19 |
| 21.51370471 | 9.1% | 93.3% | 2 | 14 | 1 | 20 |
| 30.15332726 | 9.1% | 100.0% | 2 | 15 | 0 | 20 |
| 56.92785582 | 4.5% | 100.0% | 1 | 15 | 0 | 21 |
| 166.0183046 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

M14786_8 by SAMP_GRP

| Performed by | | | | | Date | |
|--------------|--------|--------|----|----|------|----|
| 0.023475635 | 100.0% | 13.3% | 22 | 2 | 13 | 0 |
| 0.179128407 | 100.0% | 20.0% | 22 | 3 | 12 | 0 |
| 0.267044214 | 100.0% | 26.7% | 22 | 4 | 11 | 0 |
| 0.439943972 | 100.0% | 33.3% | 22 | 5 | 10 | 0 |
| 0.747059995 | 95.5% | 33.3% | 21 | 5 | 10 | 1 |
| 0.803327362 | 95.5% | 40 0% | 21 | 6 | 9 | 1 |
| 0.944758506 | 95.5% | 46.7% | 21 | 7 | 8 | 1 |
| 1.088580369 | 90.9% | 46.7% | 20 | 7 | 8 | 2 |
| 1.16040567 | 90.9% | 53.3% | 20 | 8 | 7 | 2 |
| 1.232976867 | 86.4% | 53.3% | 19 | 8 | 7 | 3 |
| 1.328282419 | 81.8% | 53.3% | 18 | 8 | 7 | 4 |
| 1.737456748 | 81.8% | 60.0% | 18 | 9 | 6 | 4 |
| 1.862991377 | 77 3% | 60.0% | 17 | 9 | 6 | 5 |
| 2.618800454 | 72.7% | 60.0% | 16 | 9 | 6 | 6 |
| 3.190489507 | 72.7% | 66.7% | 16 | 10 | 5 | 6 |
| 3.593950342 | 68.2% | 66.7% | 15 | 10 | 5 | 7 |
| 3.992662117 | 63.6% | 66.7% | 14 | 10 | 5 | 8 |
| 4.292351631 | 63 6% | 73.3% | 14 | 11 | 4 | 8 |
| 5.173824392 | 59.1% | 73.3% | 13 | 11 | 4 | 9 |
| 5.435998972 | 54.5% | 73.3% | 12 | 11 | 4 | 10 |
| 6.130557824 | 50.0% | 73.3% | 11 | 11 | 4 | 11 |
| 6.430648786 | 45.5% | 73.3% | 10 | 11 | 4 | 12 |
| 6.804374645 | 40.9% | 73.3% | 9 | 11 | 4 | 13 |
| 6.894913459 | 36.4% | 73.3% | 8 | 11 | 4 | 14 |
| 7.090966562 | 31.8% | 73 3% | 7 | 11 | 4 | 15 |
| 7.664042534 | 31.8% | 80.0% | 7 | 12 | 3 | 15 |
| 7.846086851 | 31.8% | 86.7% | 7 | 13 | 2 | 15 |
| 9.148478696 | 27 3% | 86 7% | 6 | 13 | 2 | 16 |
| 11.37402216 | 22.7% | 86.7% | 5 | 13 | 2 | 17 |
| 12.34702758 | 22.7% | 93.3% | 5 | 14 | 1 | 17 |
| 17.16718737 | 18.2% | 93.3% | 4 | 14 | 1 | 18 |
| 20.98234151 | 13.6% | 93.3% | 3 | 14 | 1 | 19 |
| 32.06067547 | 13.6% | 100.0% | 3 | 15 | 0 | 19 |
| 35.35146295 | 9.1% | 100.0% | 2 | 15 | 0 | 20 |
| 42.47069795 | 4.5% | 100.0% | 1 | 15 | 0 | 21 |
| 281.2400752 | 0.0% | 100 0% | 0 | 15 | 0 | 22 |

15.11.2019

analysed with Analyse-it + Clinical Laboratory 1 82

Test Receiver Operator Characteristic (ROC) curves

M15111_4 by SAMP_GRP

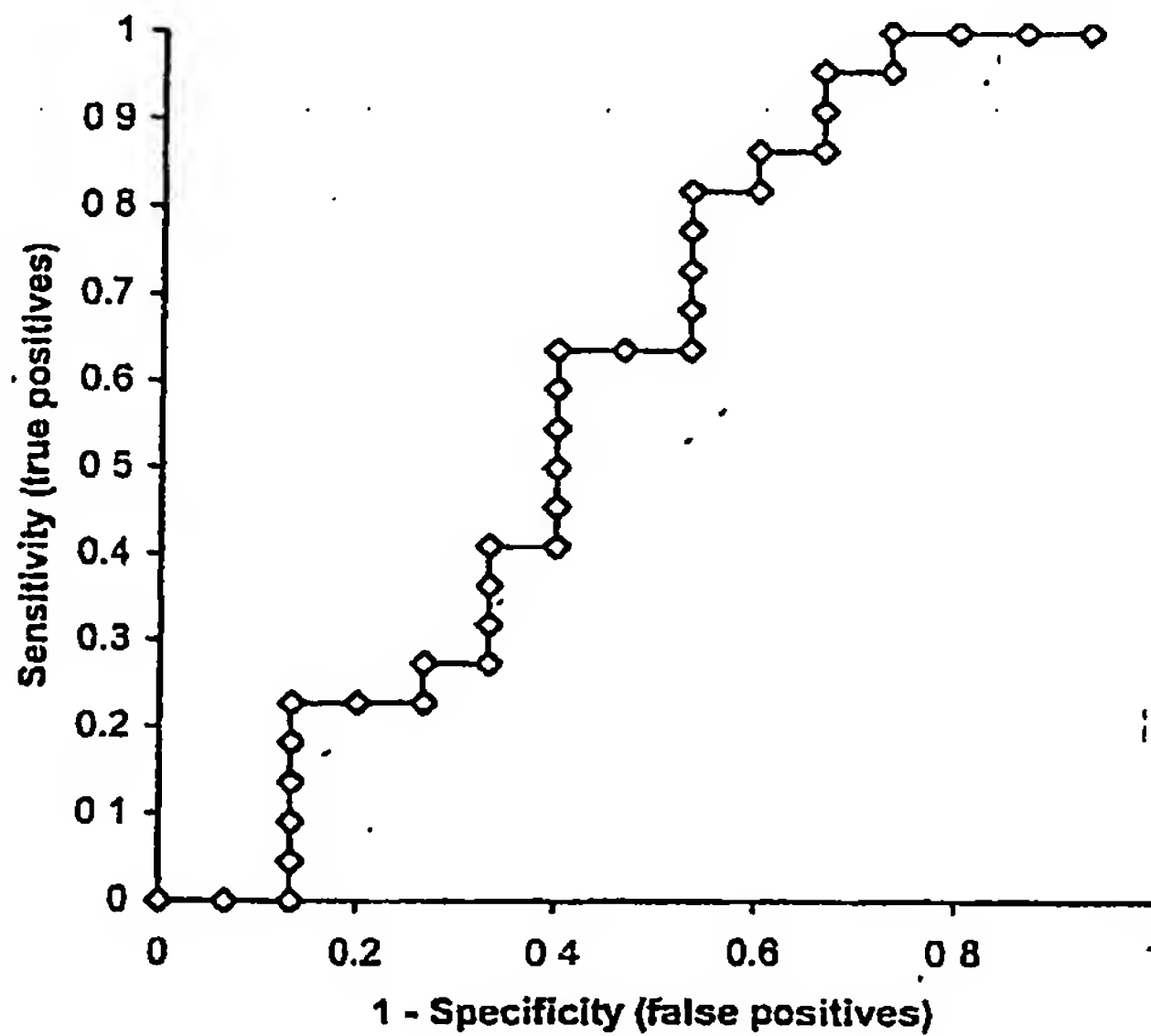
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M15111_4 | 0.603 | 0.1038 | 0.1604 | 0.400 to 0.806 | have higher values |



| M15111_4
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| -0.129346634 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

Test Receiver Operator Characteristic (ROC) curves

analysed with Analyse-It + Clinical Laboratory 1.6.2

M15111_4 by SAMP_GRP

| Performed by | | | | | Date | |
|--------------|--------|--------|----|----|------|----|
| -0.082272482 | 100.0% | 13.3% | 22 | 2 | 13 | 0 |
| -0.051647397 | 100.0% | 20.0% | 22 | 3 | 12 | 0 |
| 0.083955483 | 100.0% | 26.7% | 22 | 4 | 11 | 0 |
| 0.103130253 | 95.5% | 26.7% | 21 | 4 | 11 | 1 |
| 0.156015035 | 95.5% | 33.3% | 21 | 5 | 10 | 1 |
| 0.24131824 | 90.9% | 33.3% | 20 | 5 | 10 | 2 |
| 0.30192565 | 86.4% | 33.3% | 19 | 5 | 10 | 3 |
| 0.357009516 | 86.4% | 40.0% | 19 | 6 | 9 | 3 |
| 0.418122078 | 81.8% | 40.0% | 18 | 6 | 9 | 4 |
| 0.501114979 | 81.8% | 46.7% | 18 | 7 | 8 | 4 |
| 0.506992262 | 77.3% | 46.7% | 17 | 7 | 8 | 5 |
| 0.591501 | 72.7% | 46.7% | 16 | 7 | 8 | 6 |
| 0.625650143 | 68.2% | 46.7% | 15 | 7 | 8 | 7 |
| 0.626384321 | 63.6% | 46.7% | 14 | 7 | 8 | 8 |
| 0.632164126 | 63.6% | 53.3% | 14 | 8 | 7 | 8 |
| 0.63531719 | 63.6% | 60.0% | 14 | 9 | 6 | 8 |
| 0.645259109 | 59.1% | 60.0% | 13 | 9 | 6 | 9 |
| 0.678909306 | 54.5% | 60.0% | 12 | 9 | 6 | 10 |
| 0.840789629 | 50.0% | 60.0% | 11 | 9 | 6 | 11 |
| 0.864326107 | 45.5% | 60.0% | 10 | 9 | 6 | 12 |
| 0.961140158 | 40.9% | 60.0% | 9 | 9 | 6 | 13 |
| 1.035335892 | 40.9% | 66.7% | 9 | 10 | 5 | 13 |
| 1.36632823 | 36.4% | 66.7% | 8 | 10 | 5 | 14 |
| 1.380299287 | 31.8% | 66.7% | 7 | 10 | 5 | 15 |
| 1.803915729 | 27.3% | 66.7% | 6 | 10 | 5 | 16 |
| 1.918985561 | 27.3% | 73.3% | 6 | 11 | 4 | 16 |
| 1.959011122 | 22.7% | 73.3% | 5 | 11 | 4 | 17 |
| 2.266327269 | 22.7% | 80.0% | 5 | 12 | 3 | 17 |
| 2.75618663 | 22.7% | 86.7% | 5 | 13 | 2 | 17 |
| 3.050300348 | 18.2% | 86.7% | 4 | 13 | 2 | 18 |
| 4.376056415 | 13.6% | 86.7% | 3 | 13 | 2 | 19 |
| 4.817121905 | 9.1% | 86.7% | 2 | 13 | 2 | 20 |
| 7.363790965 | 4.5% | 86.7% | 1 | 13 | 2 | 21 |
| 9.744086366 | 0.0% | 86.7% | 0 | 13 | 2 | 22 |
| 39.88240945 | 0.0% | 93.3% | 0 | 14 | 1 | 22 |
| 161.5535104 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

15.2 kP

05/04/2007 11:03:03

analysed with Analyse-It + Clinical Laboratory 1 62

Test Receiver Operator Characteristic (ROC) curves

M15236_2 by SAMP_GRP

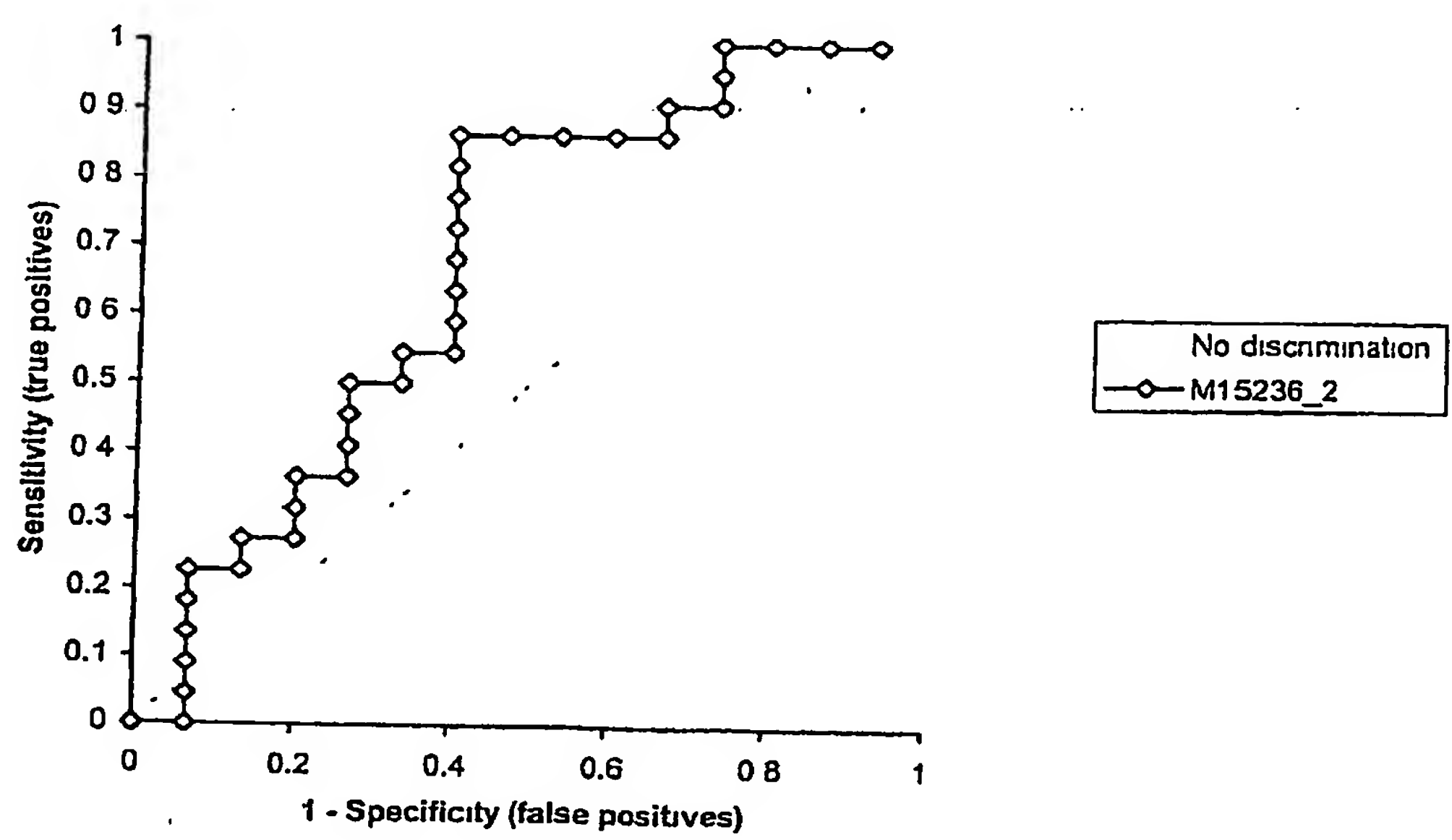
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M15236_2 | 0.685 | 0.0954 | 0.0263 | 0.498 to 0.872 | have higher values |



| M15236_2
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 0.177481002 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

Test Receiver Operator Characteristic (ROC) curves

M15236_2 by SAMP_GRP

| Performed by | Date | | | | | |
|--------------|--------|--------|----|----|----|----|
| 0.26932092 | 100.0% | 13.3% | 22 | 2 | 13 | 0 |
| 0.501614485 | 100.0% | 20.0% | 22 | 3 | 12 | 0 |
| 0.656769452 | 100.0% | 26.7% | 22 | 4 | 11 | 0 |
| 0.719916699 | 95.5% | 26.7% | 21 | 4 | 11 | 1 |
| 0.807504736 | 90.9% | 26.7% | 20 | 4 | 11 | 2 |
| 0.983183733 | 90.9% | 33.3% | 20 | 5 | 10 | 2 |
| 1.046305243 | 86.4% | 33.3% | 19 | 5 | 10 | 3 |
| 1.276111699 | 86.4% | 40.0% | 19 | 6 | 9 | 3 |
| 1.471614269 | 86.4% | 46.7% | 19 | 7 | 8 | 3 |
| 1.504545069 | 86.4% | 53.3% | 19 | 8 | 7 | 3 |
| 1.561579588 | 86.4% | 60.0% | 19 | 9 | 6 | 3 |
| 1.861941735 | 81.8% | 60.0% | 18 | 9 | 6 | 4 |
| 2.005918691 | 77.3% | 60.0% | 17 | 9 | 6 | 5 |
| 2.076209404 | 72.7% | 60.0% | 16 | 9 | 6 | 6 |
| 2.239171671 | 68.2% | 60.0% | 15 | 9 | 6 | 7 |
| 2.502252869 | 63.6% | 60.0% | 14 | 9 | 6 | 8 |
| 2.710895729 | 59.1% | 60.0% | 13 | 9 | 6 | 9 |
| 3.537996275 | 54.5% | 60.0% | 12 | 9 | 6 | 10 |
| 3.8680481 | 54.5% | 66.7% | 12 | 10 | 5 | 10 |
| 4.382965751 | 50.0% | 66.7% | 11 | 10 | 5 | 11 |
| 4.513363682 | 50.0% | 73.3% | 11 | 11 | 4 | 11 |
| 4.518159572 | 45.5% | 73.3% | 10 | 11 | 4 | 12 |
| 5.011155209 | 40.9% | 73.3% | 9 | 11 | 4 | 13 |
| 5.245641846 | 36.4% | 73.3% | 8 | 11 | 4 | 14 |
| 5.648417793 | 36.4% | 80.0% | 8 | 12 | 3 | 14 |
| 7.605043085 | 31.8% | 80.0% | 7 | 12 | 3 | 15 |
| 9.152569514 | 27.3% | 80.0% | 6 | 12 | 3 | 16 |
| 9.752635213 | 27.3% | 86.7% | 6 | 13 | 2 | 16 |
| 10.43369202 | 22.7% | 86.7% | 5 | 13 | 2 | 17 |
| 11.53556191 | 22.7% | 93.3% | 5 | 14 | 1 | 17 |
| 12.56018381 | 18.2% | 93.3% | 4 | 14 | 1 | 18 |
| 13.38389997 | 13.6% | 93.3% | 3 | 14 | 1 | 19 |
| 17.11945792 | 9.1% | 93.3% | 2 | 14 | 1 | 20 |
| 17.71010644 | 4.5% | 93.3% | 1 | 14 | 1 | 21 |
| 54.23769026 | 0.0% | 93.3% | 0 | 14 | 1 | 22 |
| 298.1897417 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

16.1 WD

analysed with Analyse-It + Clinical Laboratory 1 62

Test Receiver Operator Characteristic (ROC) curves

M16116_7 by SAMP_GRP

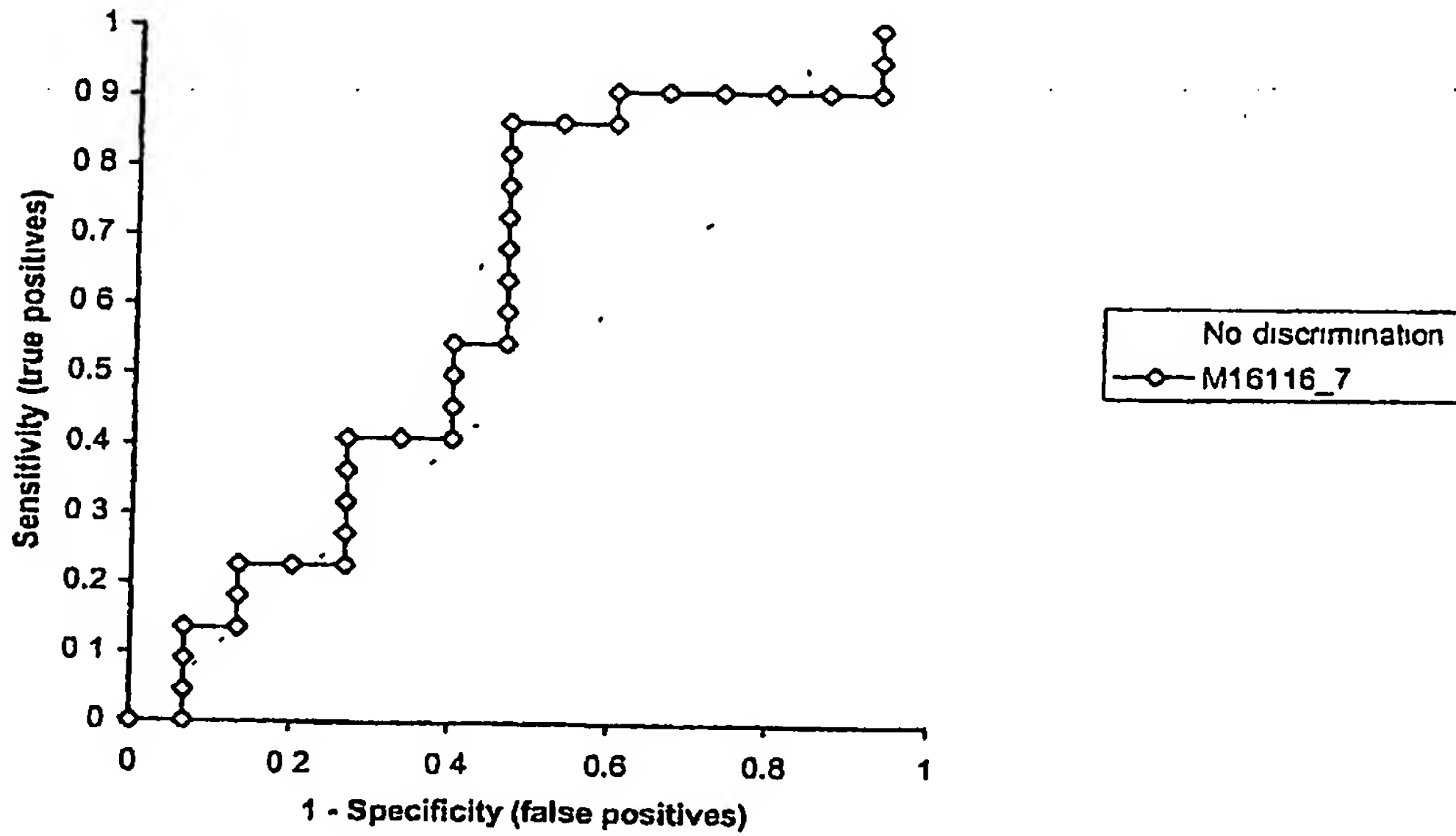
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M16116_7 | 0.615 | 0.1011 | 0.1273 | 0.417 to 0.813 | have higher values |



| M16116_7
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| -0.110846445 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

Test Receiver Operator Characteristic (ROC) curves

M16116_7 by SAMP_GRP

| Performed by | | | | | Date | |
|--------------|-------|--------|----|----|------|----|
| -0.080009221 | 95.5% | 6.7% | 21 | 1 | 14 | 1 |
| 0.13243982 | 90.9% | 6.7% | 20 | 1 | 14 | 2 |
| 0.132569031 | 90.9% | 13.3% | 20 | 2 | 13 | 2 |
| 0.132897016 | 90.9% | 20.0% | 20 | 3 | 12 | 2 |
| 0.141616725 | 90.9% | 26.7% | 20 | 4 | 11 | 2 |
| 0.191151907 | 90.9% | 33.3% | 20 | 5 | 10 | 2 |
| 0.242371361 | 90.9% | 40.0% | 20 | 6 | 9 | 2 |
| 0.292459979 | 86.4% | 40.0% | 19 | 6 | 9 | 3 |
| 0.373858157 | 86.4% | 46.7% | 19 | 7 | 8 | 3 |
| 0.401639062 | 86.4% | 53.3% | 19 | 8 | 7 | 3 |
| 0.461780418 | 81.8% | 53.3% | 18 | 8 | 7 | 4 |
| 0.472465163 | 77.3% | 53.3% | 17 | 8 | 7 | 5 |
| 0.499106112 | 72.7% | 53.3% | 16 | 8 | 7 | 6 |
| 0.504270861 | 68.2% | 53.3% | 15 | 8 | 7 | 7 |
| 0.62504857 | 63.6% | 53.3% | 14 | 8 | 7 | 8 |
| 0.720128095 | 59.1% | 53.3% | 13 | 8 | 7 | 9 |
| 0.724831498 | 54.5% | 53.3% | 12 | 8 | 7 | 10 |
| 0.899794601 | 54.5% | 60.0% | 12 | 9 | 6 | 10 |
| 0.931865595 | 50.0% | 60.0% | 11 | 9 | 6 | 11 |
| 0.9363429 | 45.5% | 60.0% | 10 | 9 | 6 | 12 |
| 0.995489407 | 40.9% | 60.0% | 9 | 9 | 6 | 13 |
| 1.135442279 | 40.9% | 66.7% | 9 | 10 | 5 | 13 |
| 1.18410198 | 40.9% | 73.3% | 9 | 11 | 4 | 13 |
| 1.280101252 | 36.4% | 73.3% | 8 | 11 | 4 | 14 |
| 1.510623299 | 31.8% | 73.3% | 7 | 11 | 4 | 15 |
| 1.519705578 | 27.3% | 73.3% | 6 | 11 | 4 | 16 |
| 1.739130465 | 22.7% | 73.3% | 5 | 11 | 4 | 17 |
| 1.739313948 | 22.7% | 80.0% | 5 | 12 | 3 | 17 |
| 1.77708523 | 22.7% | 86.7% | 5 | 13 | 2 | 17 |
| 2.036891128 | 18.2% | 86.7% | 4 | 13 | 2 | 18 |
| 2.867780521 | 13.6% | 86.7% | 3 | 13 | 2 | 19 |
| 3.247367684 | 13.6% | 93.3% | 3 | 14 | 1 | 19 |
| 3.500757425 | 9.1% | 93.3% | 2 | 14 | 1 | 20 |
| 4.574331216 | 4.5% | 93.3% | 1 | 14 | 1 | 21 |
| 6.042793811 | 0.0% | 93.3% | 0 | 14 | 1 | 22 |
| 222.0484769 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

250 WP

analysed with Analyse-it + Clinical Laboratory 1

Test Receiver Operator Characteristic (ROC) curves

M25041_2 by SAMP_GRP

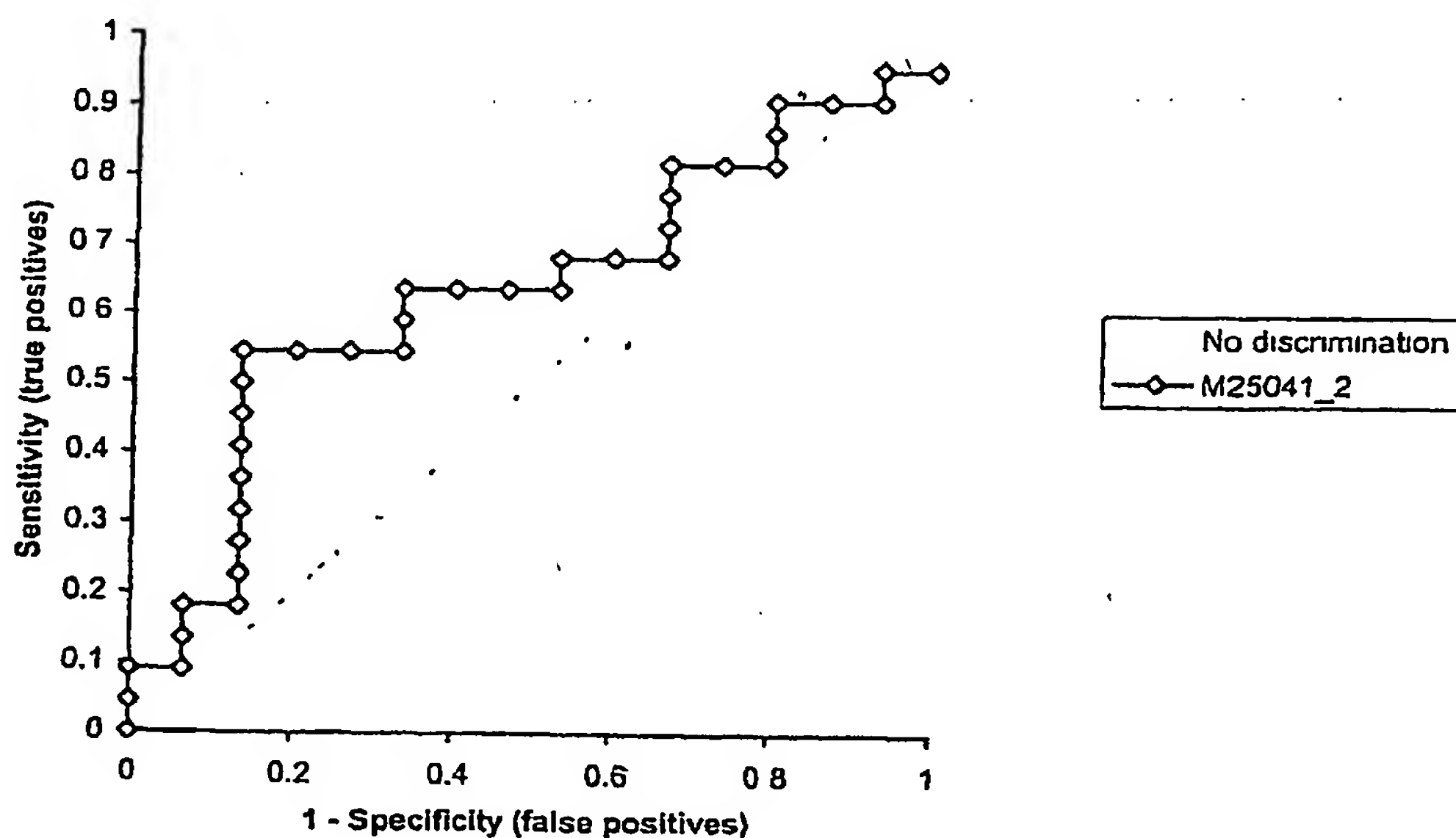
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M25041_2 | 0.639 | 0.0933 | 0.0675 | 0.457 to 0.822 | have higher values |



| M25041_2
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 0.793645654 | 95.5% | 0.0% | 21 | 0 | 15 | 1 |

Test Receiver Operator Characteristic (ROC) curves

M25041_2 by SAMP_GRP

| Performed by | | | | | | Date | |
|--------------|-------|--------|----|----|----|------|--|
| 0.817153162 | 95.5% | 6.7% | 21 | 1 | 14 | 1 | |
| 1.082548537 | 90.9% | 6.7% | 20 | 1 | 14 | 2 | |
| 1.141165731 | 90.9% | 13.3% | 20 | 2 | 13 | 2 | |
| 1.237989017 | 90.9% | 20.0% | 20 | 3 | 12 | 2 | |
| 1.25499662 | 86.4% | 20.0% | 19 | 3 | 12 | 3 | |
| 1.343229757 | 81.8% | 20.0% | 18 | 3 | 12 | 4 | |
| 1.349329152 | 81.8% | 26.7% | 18 | 4 | 11 | 4 | |
| 2.081998999 | 81.8% | 33.3% | 18 | 5 | 10 | 4 | |
| 2.20479043 | 77.3% | 33.3% | 17 | 5 | 10 | 5 | |
| 2.232456456 | 72.7% | 33.3% | 16 | 5 | 10 | 6 | |
| 2.436031979 | 68.2% | 33.3% | 15 | 5 | 10 | 7 | |
| 2.577796281 | 68.2% | 40.0% | 15 | 6 | 9 | 7 | |
| 3.022638023 | 68.2% | 46.7% | 15 | 7 | 8 | 7 | |
| 3.292505173 | 63.6% | 46.7% | 14 | 7 | 8 | 8 | |
| 3.378232079 | 63.6% | 53.3% | 14 | 8 | 7 | 8 | |
| 3.569749296 | 63.6% | 60.0% | 14 | 9 | 6 | 8 | |
| 3.947644366 | 63.6% | 66.7% | 14 | 10 | 5 | 8 | |
| 4.017402491 | 59.1% | 66.7% | 13 | 10 | 5 | 9 | |
| 4.025797474 | 54.5% | 66.7% | 12 | 10 | 5 | 10 | |
| 4.641249207 | 54.5% | 73.3% | 12 | 11 | 4 | 10 | |
| 4.672013348 | 54.5% | 80.0% | 12 | 12 | 3 | 10 | |
| 5.0163702 | 54.5% | 86.7% | 12 | 13 | 2 | 10 | |
| 5.51431751 | 50.0% | 86.7% | 11 | 13 | 2 | 11 | |
| 6.121226492 | 45.5% | 86.7% | 10 | 13 | 2 | 12 | |
| 6.421619338 | 40.9% | 86.7% | 9 | 13 | 2 | 13 | |
| 6.493739417 | 36.4% | 86.7% | 8 | 13 | 2 | 14 | |
| 7.12459442 | 31.8% | 86.7% | 7 | 13 | 2 | 15 | |
| 9.376347689 | 27.3% | 86.7% | 6 | 13 | 2 | 16 | |
| 11.87108569 | 22.7% | 86.7% | 5 | 13 | 2 | 17 | |
| 12.68431208 | 18.2% | 86.7% | 4 | 13 | 2 | 18 | |
| 12.84424644 | 18.2% | 93.3% | 4 | 14 | 1 | 18 | |
| 16.49781271 | 13.6% | 93.3% | 3 | 14 | 1 | 19 | |
| 18.59015054 | 9.1% | 93.3% | 2 | 14 | 1 | 20 | |
| 23.26913367 | 9.1% | 100.0% | 2 | 15 | 0 | 20 | |
| 26.37159816 | 4.5% | 100.0% | 1 | 15 | 0 | 21 | |
| 34.36259113 | 0.0% | 100.0% | 0 | 15 | 0 | 22 | |

280 WP

M28013_1 by SAMP_GRP

Date

SAMP_GRP

n

0

15

1

22

Curve

Area

SE

p

95% CI of Area

SAMP_GRP = 1

M28013_1

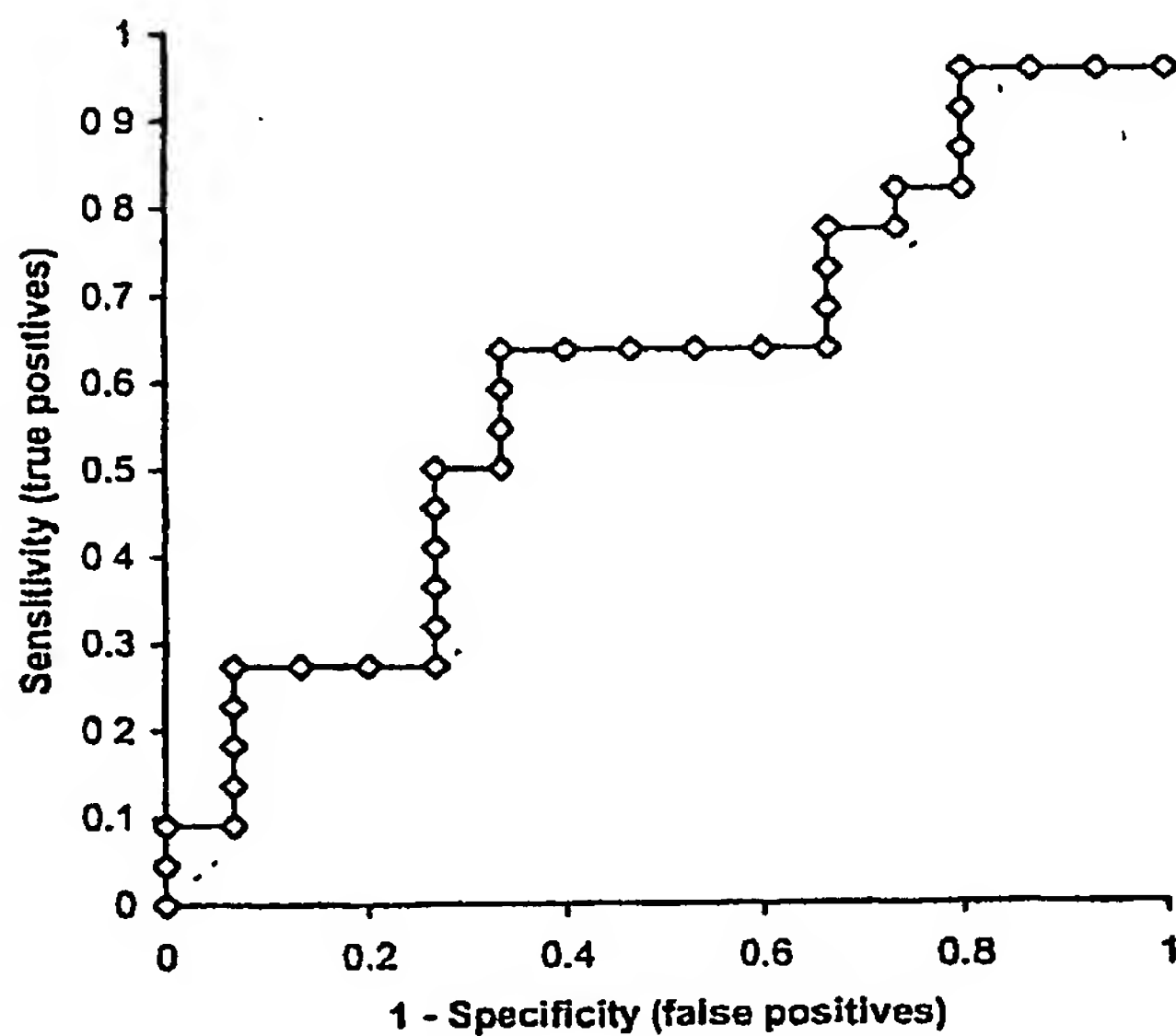
0 603

0 0954

0 1401

0.416 to 0.790

have higher values



No discrimination

- M28013_1

M28013_1

(abnormals above cut-off)

Sensitivity

Specificity

TP

TN

FP

FN

-0.095035313

95.5%

0.0%

21

0

15

1

| Test | Receiver Operator Characteristic (ROC) curves | | | | | |
|--------------|---|--------|----|----|----|------|
| | M28013_1 by SAMP_GRP | | | | | |
| Performed by | | | | | | Date |
| 0.008319371 | 95.5% | 6.7% | 21 | 1 | 14 | 1 |
| 0.010549266 | 95.5% | 13.3% | 21 | 2 | 13 | 1 |
| 0.102216294 | 95.5% | 20.0% | 21 | 3 | 12 | 1 |
| 0.113828147 | 90.9% | 20.0% | 20 | 3 | 12 | 2 |
| 0.1191118 | 86.4% | 20.0% | 19 | 3 | 12 | 3 |
| 0.126751464 | 81.8% | 20.0% | 18 | 3 | 12 | 4 |
| 0.139219149 | 81.8% | 26.7% | 18 | 4 | 11 | 4 |
| 0.143262373 | 77.3% | 26.7% | 17 | 4 | 11 | 5 |
| 0.159400568 | 77.3% | 33.3% | 17 | 5 | 10 | 5 |
| 0.175599876 | 72.7% | 33.3% | 16 | 5 | 10 | 6 |
| 0.237338251 | 68.2% | 33.3% | 15 | 5 | 10 | 7 |
| 0.253741367 | 63.6% | 33.3% | 14 | 5 | 10 | 8 |
| 0.261407068 | 63.6% | 40.0% | 14 | 6 | 9 | 8 |
| 0.275595468 | 63.6% | 46.7% | 14 | 7 | 8 | 8 |
| 0.282158382 | 63.6% | 53.3% | 14 | 8 | 7 | 8 |
| 0.297729343 | 63.6% | 60.0% | 14 | 9 | 6 | 8 |
| 0.313257239 | 63.6% | 66.7% | 14 | 10 | 5 | 8 |
| 0.323071775 | 59.1% | 66.7% | 13 | 10 | 5 | 9 |
| 0.414240943 | 54.5% | 66.7% | 12 | 10 | 5 | 10 |
| 0.431505021 | 50.0% | 66.7% | 11 | 10 | 5 | 11 |
| 0.4509231 | 50.0% | 73.3% | 11 | 11 | 4 | 11 |
| 0.46992756 | 45.5% | 73.3% | 10 | 11 | 4 | 12 |
| 0.560326976 | 40.9% | 73.3% | 9 | 11 | 4 | 13 |
| 0.697047262 | 36.4% | 73.3% | 8 | 11 | 4 | 14 |
| 0.8010417 | 31.8% | 73.3% | 7 | 11 | 4 | 15 |
| 1.017133662 | 27.3% | 73.3% | 6 | 11 | 4 | 16 |
| 1.019696331 | 27.3% | 80.0% | 6 | 12 | 3 | 16 |
| 1.023129053 | 27.3% | 86.7% | 6 | 13 | 2 | 16 |
| 1.053132432 | 27.3% | 93.3% | 6 | 14 | 1 | 16 |
| 1.26765639 | 22.7% | 93.3% | 5 | 14 | 1 | 17 |
| 2.161821389 | 18.2% | 93.3% | 4 | 14 | 1 | 18 |
| 2.231947361 | 13.6% | 93.3% | 3 | 14 | 1 | 19 |
| 2.681779385 | 9.1% | 93.3% | 2 | 14 | 1 | 20 |
| 4.009571403 | 9.1% | 100.0% | 2 | 15 | 0 | 20 |
| 5.061125972 | 4.5% | 100.0% | 1 | 15 | 0 | 21 |
| 21.26275531 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

Test Receiver Operator Characteristic (ROC) curves

M49972_1 by SAMP_GRP

| Performed by | | Date | | | | |
|--------------|--------|--------|----|----|----|----|
| 0.132950234 | 100.0% | 13.3% | 22 | 2 | 13 | 0 |
| 0.141985312 | 100.0% | 20.0% | 22 | 3 | 12 | 0 |
| 0.246235855 | 95.5% | 20.0% | 21 | 3 | 12 | 1 |
| 0.287564918 | 95.5% | 26.7% | 21 | 4 | 11 | 1 |
| 0.293882443 | 95.5% | 33.3% | 21 | 5 | 10 | 1 |
| 0.306763535 | 95.5% | 40.0% | 21 | 6 | 9 | 1 |
| 0.349275179 | 95.5% | 46.7% | 21 | 7 | 8 | 1 |
| 0.372101499 | 90.9% | 46.7% | 20 | 7 | 8 | 2 |
| 0.523240205 | 86.4% | 46.7% | 19 | 7 | 8 | 3 |
| 0.529789658 | 81.8% | 46.7% | 18 | 7 | 8 | 4 |
| 0.532304145 | 77.3% | 46.7% | 17 | 7 | 8 | 5 |
| 0.565558298 | 77.3% | 53.3% | 17 | 8 | 7 | 5 |
| 0.615696638 | 72.7% | 53.3% | 16 | 8 | 7 | 6 |
| 0.655358293 | 72.7% | 60.0% | 16 | 9 | 6 | 6 |
| 0.708502864 | 68.2% | 60.0% | 15 | 9 | 6 | 7 |
| 0.820163109 | 63.6% | 60.0% | 14 | 9 | 6 | 8 |
| 0.829209887 | 59.1% | 60.0% | 13 | 9 | 6 | 9 |
| 0.889935695 | 59.1% | 66.7% | 13 | 10 | 5 | 9 |
| 0.900952491 | 59.1% | 73.3% | 13 | 11 | 4 | 9 |
| 0.952218444 | 54.5% | 73.3% | 12 | 11 | 4 | 10 |
| 0.963450793 | 50.0% | 73.3% | 11 | 11 | 4 | 11 |
| 1.053272294 | 50.0% | 80.0% | 11 | 12 | 3 | 11 |
| 1.115031656 | 45.5% | 80.0% | 10 | 12 | 3 | 12 |
| 1.117385785 | 40.9% | 80.0% | 9 | 12 | 3 | 13 |
| 1.231643564 | 36.4% | 80.0% | 8 | 12 | 3 | 14 |
| 1.369123003 | 36.4% | 86.7% | 8 | 13 | 2 | 14 |
| 1.421508865 | 31.8% | 86.7% | 7 | 13 | 2 | 15 |
| 1.460854582 | 27.3% | 86.7% | 6 | 13 | 2 | 16 |
| 1.795777414 | 22.7% | 86.7% | 5 | 13 | 2 | 17 |
| 1.92994641 | 18.2% | 86.7% | 4 | 13 | 2 | 18 |
| 2.206108575 | 13.6% | 86.7% | 3 | 13 | 2 | 19 |
| 2.278575727 | 13.6% | 93.3% | 3 | 14 | 1 | 19 |
| 2.610392714 | 9.1% | 93.3% | 2 | 14 | 1 | 20 |
| 2.849559837 | 4.5% | 93.3% | 1 | 14 | 1 | 21 |
| 5.589760177 | 4.5% | 100.0% | 1 | 15 | 0 | 21 |
| 27.19836861 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

Test Receiver Operator Characteristic (ROC) curves

M50078_2 by SAMP_GRP

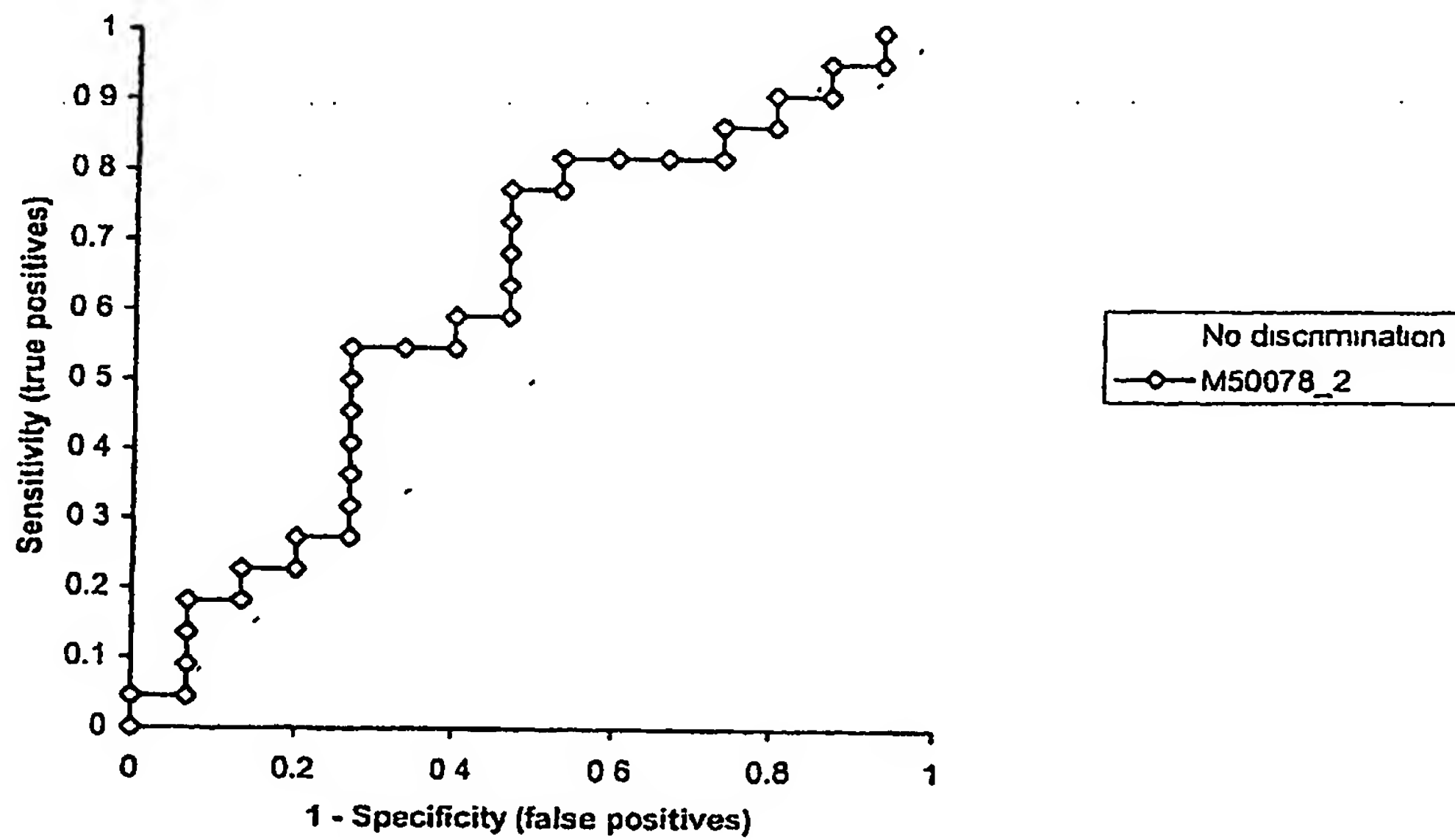
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M50078_2 | 0.624 | 0.0966 | 0.0993 | 0.435 to 0.814 | have higher values |



| M50078_2
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 0.083771249 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

Test Receiver Operator Characteristic (ROC) curves

M50078_2 by SAMP_GRP

| Performed by | Date | | | | | |
|--------------|-------|--------|----|----|----|----|
| 0.112192966 | 95.5% | 6.7% | 21 | 1 | 14 | 1 |
| 0.187614661 | 95.5% | 13.3% | 21 | 2 | 13 | 1 |
| 0.249307343 | 90.9% | 13.3% | 20 | 2 | 13 | 2 |
| 0.263981414 | 90.9% | 20.0% | 20 | 3 | 12 | 2 |
| 0.306532284 | 86.4% | 20.0% | 19 | 3 | 12 | 3 |
| 0.338598049 | 86.4% | 26.7% | 19 | 4 | 11 | 3 |
| 0.345538383 | 81.8% | 26.7% | 18 | 4 | 11 | 4 |
| 0.39682968 | 81.8% | 33.3% | 18 | 5 | 10 | 4 |
| 0.418253613 | 81.8% | 40.0% | 18 | 6 | 9 | 4 |
| 0.433207988 | 81.8% | 46.7% | 18 | 7 | 8 | 4 |
| 0.442596153 | 77.3% | 46.7% | 17 | 7 | 8 | 5 |
| 0.523921441 | 77.3% | 53.3% | 17 | 8 | 7 | 5 |
| 0.533559718 | 72.7% | 53.3% | 16 | 8 | 7 | 6 |
| 0.580795124 | 68.2% | 53.3% | 15 | 8 | 7 | 7 |
| 0.591320318 | 63.6% | 53.3% | 14 | 8 | 7 | 8 |
| 0.66716828 | 59.1% | 53.3% | 13 | 8 | 7 | 9 |
| 0.673010393 | 59.1% | 60.0% | 13 | 9 | 6 | 9 |
| 0.749027671 | 54.5% | 60.0% | 12 | 9 | 6 | 10 |
| 0.762425926 | 54.5% | 66.7% | 12 | 10 | 5 | 10 |
| 0.795540626 | 54.5% | 73.3% | 12 | 11 | 4 | 10 |
| 0.841469072 | 50.0% | 73.3% | 11 | 11 | 4 | 11 |
| 0.887016568 | 45.5% | 73.3% | 10 | 11 | 4 | 12 |
| 0.936274853 | 40.9% | 73.3% | 9 | 11 | 4 | 13 |
| 1.151312518 | 36.4% | 73.3% | 8 | 11 | 4 | 14 |
| 1.511400676 | 31.8% | 73.3% | 7 | 11 | 4 | 15 |
| 1.530864328 | 27.3% | 73.3% | 6 | 11 | 4 | 16 |
| 1.698991556 | 27.3% | 80.0% | 6 | 12 | 3 | 16 |
| 1.701630079 | 22.7% | 80.0% | 5 | 12 | 3 | 17 |
| 1.738942865 | 22.7% | 86.7% | 5 | 13 | 2 | 17 |
| 1.742833851 | 18.2% | 86.7% | 4 | 13 | 2 | 18 |
| 1.752666622 | 18.2% | 93.3% | 4 | 14 | 1 | 18 |
| 2.427706313 | 13.6% | 93.3% | 3 | 14 | 1 | 19 |
| 2.677791701 | 9.1% | 93.3% | 2 | 14 | 1 | 20 |
| 2.690070914 | 4.5% | 93.3% | 1 | 14 | 1 | 21 |
| 2.911184998 | 4.5% | 100.0% | 1 | 15 | 0 | 21 |
| 18.44471648 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

Test | Receiver Operator Characteristic (ROC) curves

M51107_4 by SAMP_GRP

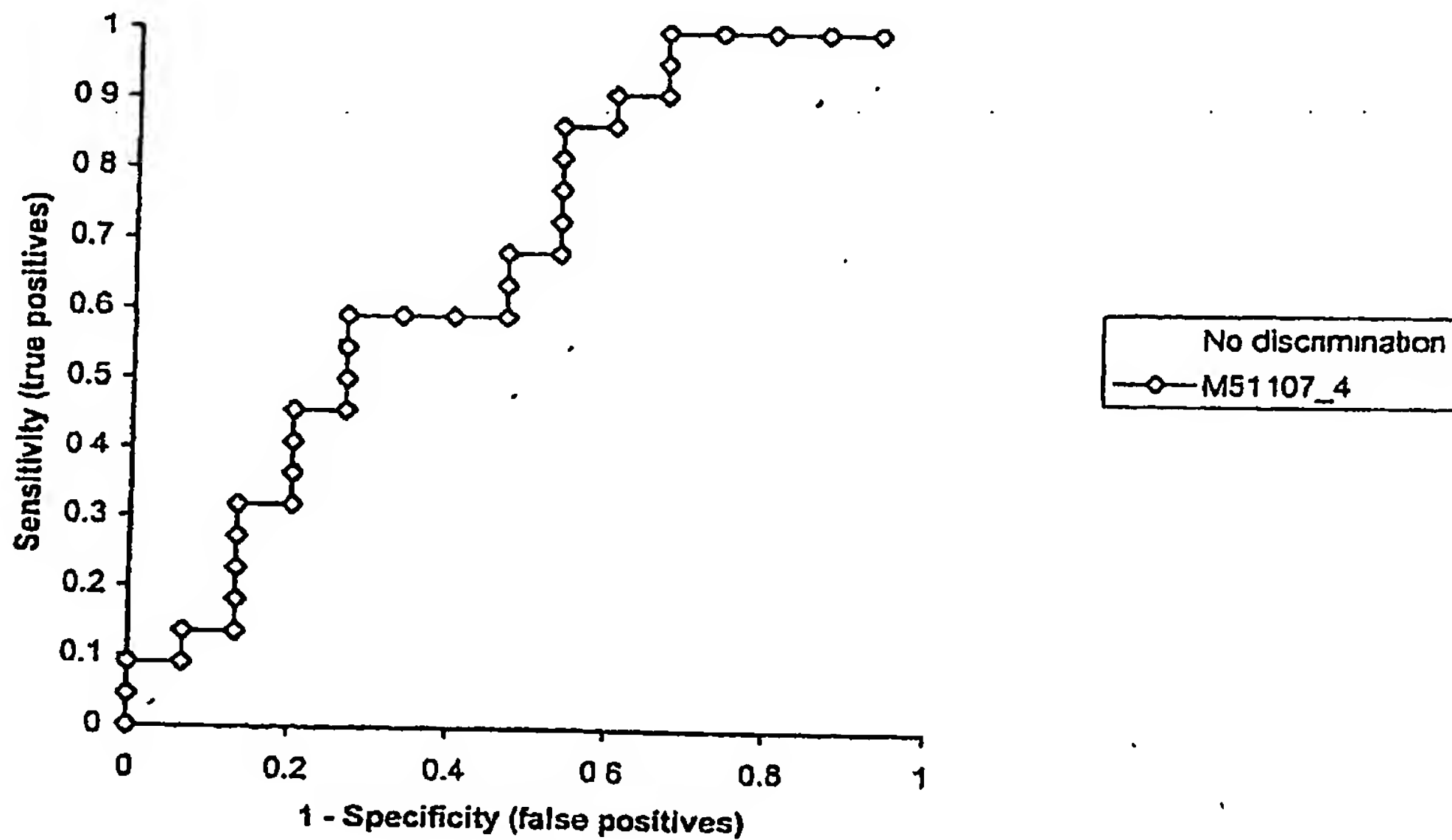
Performed by

Date _____

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M51107_4 | 0.682 | 0.0934 | 0.0258 | 0.499 to 0.865 | have higher values |



| M51107_4
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 0.074699264 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

M51107_4 by SAMP_GRP

128

5/3/12

Test Receiver Operator Characteristic (ROC) curves

analysed with Analyse-it + Clinical Laboratory 1 62

M51349_5 by SAMP_GRP

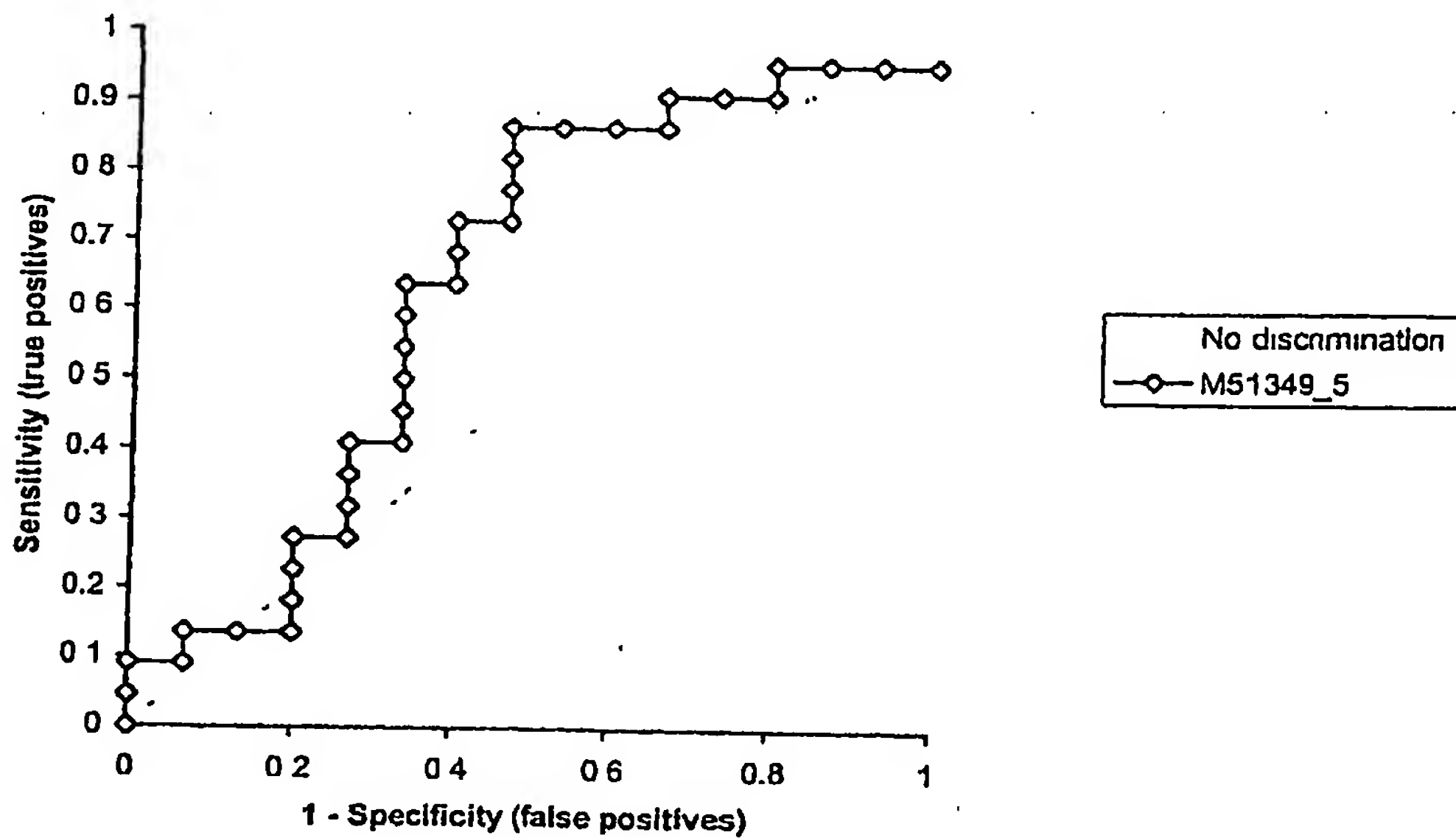
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M51349_5 | 0.645 | 0.0987 | 0.0704 | 0.452 to 0.839 | have higher values |



| M51349_5
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 0.200166025 | 95.5% | 0.0% | 21 | 0 | 15 | 1 |

Test Receiver Operator Characteristic (ROC) curves

M51349_5 by SAMP_GRP

| Performed by | Date | | | | | |
|--------------|-------|--------|----|----|----|----|
| 0.24300717 | 95.5% | 6 7% | 21 | 1 | 14 | 1 |
| 0.276544758 | 95.5% | 13 3% | 21 | 2 | 13 | 1 |
| 0.407583283 | 95.5% | 20.0% | 21 | 3 | 12 | 1 |
| 0.468872073 | 90.9% | 20.0% | 20 | 3 | 12 | 2 |
| 0.50797997 | 90.9% | 26.7% | 20 | 4 | 11 | 2 |
| 0.524022195 | 90.9% | 33.3% | 20 | 5 | 10 | 2 |
| 0.553829455 | 86.4% | 33.3% | 19 | 5 | 10 | 3 |
| 0.632492332 | 86.4% | 40.0% | 19 | 6 | 9 | 3 |
| 0.668511881 | 86.4% | 46.7% | 19 | 7 | 8 | 3 |
| 0.72469887 | 86.4% | 53.3% | 19 | 8 | 7 | 3 |
| 0.898878277 | 81 8% | 53 3% | 18 | 8 | 7 | 4 |
| 1.029316771 | 77.3% | 53.3% | 17 | 8 | 7 | 5 |
| 1.075690064 | 72.7% | 53.3% | 16 | 8 | 7 | 6 |
| 1.089240673 | 72.7% | 60.0% | 16 | 9 | 6 | 6 |
| 1.114174748 | 68.2% | 60.0% | 15 | 9 | 6 | 7 |
| 1.121500907 | 63.6% | 60.0% | 14 | 9 | 6 | 8 |
| 1.249953453 | 63.6% | 66.7% | 14 | 10 | 5 | 8 |
| 1.288068701 | 59 1% | 66.7% | 13 | 10 | 5 | 9 |
| 1.602950201 | 54.5% | 66.7% | 12 | 10 | 5 | 10 |
| 1.607855826 | 50.0% | 66.7% | 11 | 10 | 5 | 11 |
| 1.647088646 | 45 5% | 66.7% | 10 | 10 | 5 | 12 |
| 1.746212668 | 40.9% | 66.7% | 9 | 10 | 5 | 13 |
| 1.951038891 | 40 9% | 73.3% | 9 | 11 | 4 | 13 |
| 2.009460734 | 36.4% | 73.3% | 8 | 11 | 4 | 14 |
| 2.05487892 | 31.8% | 73.3% | 7 | 11 | 4 | 15 |
| 2.427358406 | 27.3% | 73.3% | 6 | 11 | 4 | 16 |
| 2.511947452 | 27.3% | 80 0% | 6 | 12 | 3 | 16 |
| 2.798550882 | 22.7% | 80.0% | 5 | 12 | 3 | 17 |
| 2.924870548 | 18.2% | 80.0% | 4 | 12 | 3 | 18 |
| 3.300701226 | 13.6% | 80.0% | 3 | 12 | 3 | 19 |
| 3.830189124 | 13 6% | 86.7% | 3 | 13 | 2 | 19 |
| 4.333103562 | 13.6% | 93.3% | 3 | 14 | 1 | 19 |
| 5.408541047 | 9.1% | 93.3% | 2 | 14 | 1 | 20 |
| 6.411934306 | 9.1% | 100.0% | 2 | 15 | 0 | 20 |
| 12.05457475 | 4.5% | 100.0% | 1 | 15 | 0 | 21 |
| 34.56426486 | 0.0% | 100.0% | 0 | 15 | 0 | 22 |

Test | Receiver Operator Characteristic (ROC) curves

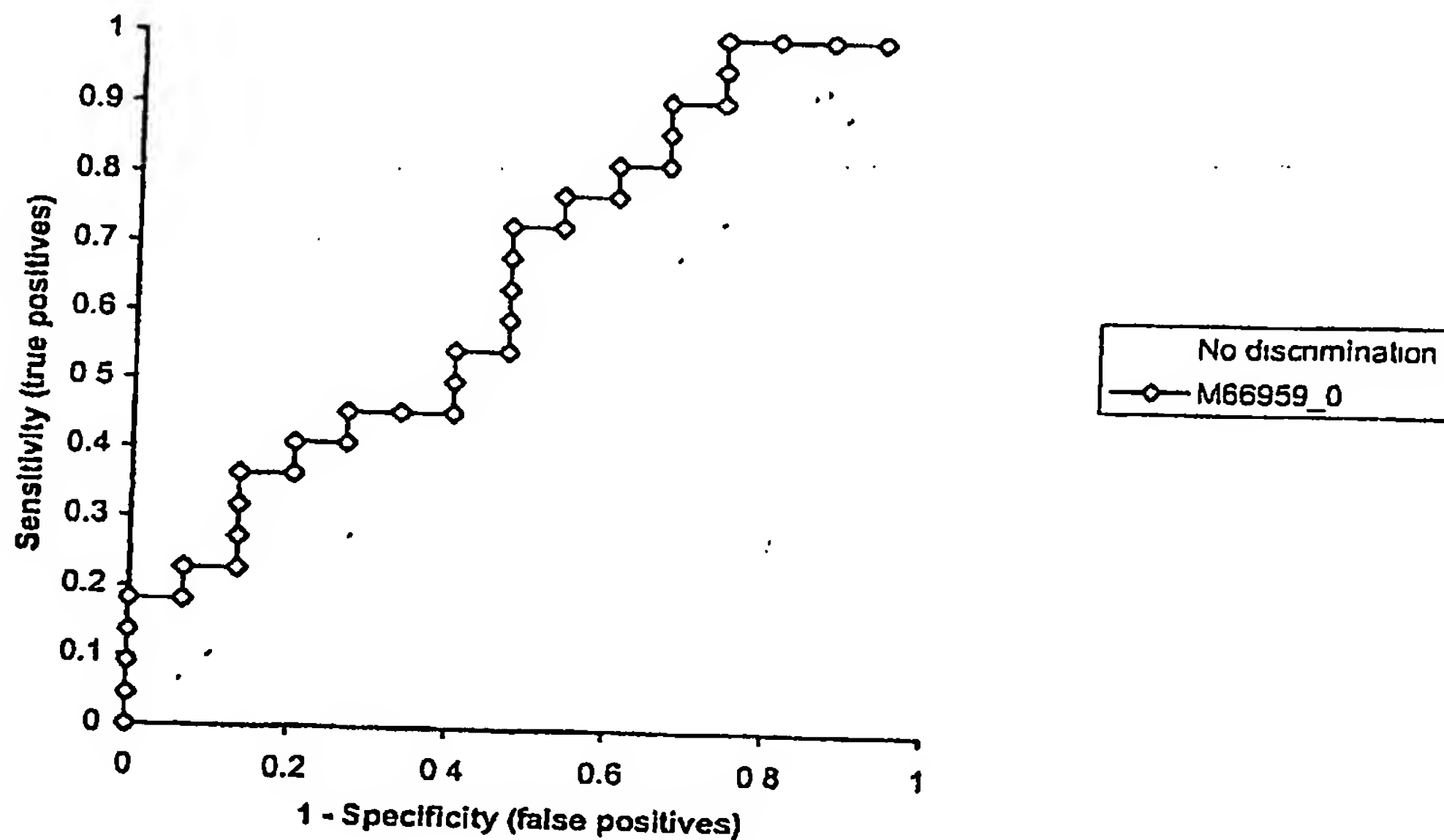
Performed by

Date

n | 37

| SAMP_GRP | n |
|----------|----|
| 0 | 15 |
| 1 | 22 |

| Curve | Area | SE | p | 95% CI of Area | SAMP_GRP = 1 |
|----------|-------|--------|--------|----------------|--------------------|
| M66959_0 | 0.658 | 0.0926 | 0.0445 | 0.476 to 0.839 | have higher values |



| M66959_0
(abnormals above cut-off) | Sensitivity | Specificity | TP | TN | FP | FN |
|---------------------------------------|-------------|-------------|----|----|----|----|
| 0.053847504 | 100.0% | 6.7% | 22 | 1 | 14 | 0 |

M66959_0 by SAMP_GRP

| Performed by | | | | | | Date | |
|--------------|--------|--------|----|----|----|------|--|
| 0.109620497 | 100.0% | 13.3% | 22 | 2 | 13 | 0 | |
| 0.145348123 | 100.0% | 20 0% | 22 | 3 | 12 | 0 | |
| 0.154709652 | 100.0% | 26.7% | 22 | 4 | 11 | 0 | |
| 0.163431718 | 95.5% | 26.7% | 21 | 4 | 11 | 1 | |
| 0.166354524 | 90.9% | 26.7% | 20 | 4 | 11 | 2 | |
| 0.186467289 | 90.9% | 33.3% | 20 | 5 | 10 | 2 | |
| 0.219563493 | 86.4% | 33.3% | 19 | 5 | 10 | 3 | |
| 0.231184488 | 81 8% | 33.3% | 18 | 5 | 10 | 4 | |
| 0.253045556 | 81.8% | 40.0% | 18 | 6 | 9 | 4 | |
| 0.26206 | 77.3% | 40.0% | 17 | 6 | 9 | 5 | |
| 0.268399456 | 77.3% | 46.7% | 17 | 7 | 8 | 5 | |
| 0.286072607 | 72.7% | 46.7% | 16 | 7 | 8 | 6 | |
| 0.290123221 | 72.7% | 53.3% | 16 | 8 | 7 | 6 | |
| 0.305445727 | 68.2% | 53.3% | 15 | 8 | 7 | 7 | |
| 0.307085278 | 63.6% | 53.3% | 14 | 8 | 7 | 8 | |
| 0.339115437 | 59.1% | 53.3% | 13 | 8 | 7 | 9 | |
| 0.34631703 | 54.5% | 53.3% | 12 | 8 | 7 | 10 | |
| 0.382061205 | 54 5% | 60.0% | 12 | 9 | 6 | 10 | |
| 0.409515884 | 50.0% | 60.0% | 11 | 9 | 6 | 11 | |
| 0.423831733 | 45.5% | 60 0% | 10 | 9 | 6 | 12 | |
| 0.448975118 | 45.5% | 66.7% | 10 | 10 | 5 | 12 | |
| 0.467458457 | 45.5% | 73.3% | 10 | 11 | 4 | 12 | |
| 0.515844068 | 40.9% | 73.3% | 9 | 11 | 4 | 13 | |
| 0.518867449 | 40.9% | 80 0% | 9 | 12 | 3 | 13 | |
| 0.525211053 | 36.4% | 80.0% | 8 | 12 | 3 | 14 | |
| 0.562143936 | 36.4% | 86.7% | 8 | 13 | 2 | 14 | |
| 0.565406222 | 31.8% | 86.7% | 7 | 13 | 2 | 15 | |
| 0.773873943 | 27.3% | 86.7% | 6 | 13 | 2 | 16 | |
| 0.868229793 | 22.7% | 86.7% | 5 | 13 | 2 | 17 | |
| 1.024396807 | 22.7% | 93.3% | 5 | 14 | 1 | 17 | |
| 1.086151053 | 18.2% | 93.3% | 4 | 14 | 1 | 18 | |
| 1.2985479 | 18.2% | 100.0% | 4 | 15 | 0 | 18 | |
| 1.628046623 | 13.6% | 100.0% | 3 | 15 | 0 | 19 | |
| 1.853453489 | 9.1% | 100.0% | 2 | 15 | 0 | 20 | |
| 2.12018388 | 4.5% | 100.0% | 1 | 15 | 0 | 21 | |
| 3.039643834 | 0.0% | 100.0% | 0 | 15 | 0 | 22 | |